



Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number:

0 393 911
A1

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: 90303859.4

(51) Int. Cl.5: C07D 263/44, C07D 413/04,
C07D 413/12, C07D 495/10,
A01N 43/76

(22) Date of filing: 10.04.90

(30) Priority: 21.04.89 US 341741
21.04.89 US 341742

(43) Date of publication of application:
24.10.90 Bulletin 90/43

(84) Designated Contracting States:
GR

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(54) Fungicidal oxazolidinones.

(57) A method of controlling plant disease using thioxooxazolidinones, oxazolidinediones and related heterocycles, some of which are new, and agriculturally suitable compositions containing them.

EP 0 393 911 A1

FUNGICIDAL OXAZOLIDINONES

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of our copending application U.S. Serial No. 07/341,741, filed
5 on April 21, 1989.

BACKGROUND OF THE INVENTION

10 This invention pertains to a novel method-of-use of compounds of Structure I as fungicides for protecting plants from disease.

Processes for the preparation of the compounds described in this invention are disclosed in the following references:

- 15 Geffken, D.; Z. Naturforsch., 1983, 38b, 1008
 Geffken, D.; Zinner, G.; Chem. Ber., 1973, 106, 2246
 Geffken, D.; Arch. Pharm., 1982, 315, 802;
 Geffken, D. Z. Naturforsch., 1987, 42b, 1202

No particular utility for the compounds is described in the above references.

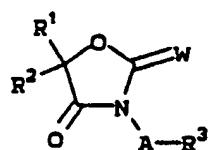
20 A new process for the preparation of these compounds is also disclosed in this application.

Compounds related to I are broadly disclosed as medicines, agrochemicals and microbicides in Japanese Patent 61/200978-A, and as general biocides in EP 249328-A. However, these applications do not encompass compounds of the instant invention, nor do they suggest the use of the compounds of this invention as fungicides particularly effective for the protection of crops against disease.

25

SUMMARY OF THE INVENTION

30 This invention comprises a method of controlling fungus disease in plants that comprises treating the locus to be protected with an effective amount of a compound of Formula I,



I

40

wherein:

A is O or NR⁴;

W is O or S;

45 R¹ is H; C₁ to C₆ alkyl; C₁ to C₆ haloalkyl; C₃ to C₆ cycloalkyl; C₂ to C₆ alkenyl; C₂ to C₆ alkynyl; C₂ to C₆ alkoxyalkyl; C₁ to C₃ alkyl substituted with C₃ to C₆ cycloalkyl, phenyl or benzyl, wherein said phenyl or benzyl ring is substituted on the ring with R⁶, and the benzylic carbon is substituted with R⁷;

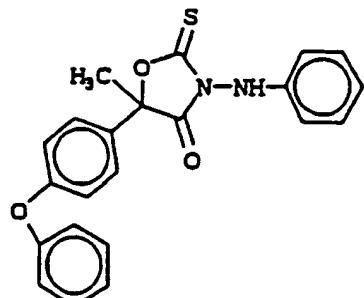
R² is phenyl substituted with R⁵ and R⁶; naphthyl substituted with 1 to 2 groups selected from R⁶; thiienyl substituted with R⁵ and R⁶; furyl substituted with R⁶; pyridyl substituted with one of the following:

50 R⁶, phenoxy substituted with R⁶, or phenylthio substituted with R⁶;
 C₁ to C₂ alkyl substituted with phenoxy or phenylthio, said phenoxy or phenylthio being substituted on the ring with R⁶;
 C₁ to C₆ alkyl; or
 C₅ to C₇ cycloalkyl; and

- R¹ and R² can be taken together, along with the carbon to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5 to 7 ring atoms in which the heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; and the carbocyclic ring can be fused with 1 or 2 R⁵-substituted benzene rings or with an R⁶-substituted thiophene ring;
- 5 R³ is phenyl substituted with R¹⁰; benzyl substituted on the benzylic carbon with a group selected from R⁷ and substituted on the phenyl ring with R¹⁰; naphthyl substituted with R¹⁰; additionally, R³ can be thienyl substituted with R¹⁰, furyl substituted with R¹⁰, pyridyl substituted with R¹⁰, pyrimidyl substituted with R¹⁰, or pyridazyl substituted with R¹⁰; or R³ can be C₂ to C₁₀ alkyl or C₅ to C₇ cycloalkyl;
- 10 R⁴ is hydrogen; formyl; C₂ to C₄ alkylcarbonyl; C₂ to C₄ haloalkylcarbonyl; C₂ to C₄ alkoxyalkylcarbonyl; C₂ to C₄ alkoxy carbonyl; C₂ to C₅ alkylaminocarbonyl; C₁ to C₄ alkylsulfonyl; C₁ to C₄ alkyl; C₄ to C₆ cycloalkyl; phenylaminocarbonyl where said phenyl is substituted with R¹⁰; and R⁴ can be C₃ to C₄ alkenyl or C₃ to C₄ alkynyl; or
- R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a pyrrolidino, piperidino or pyrrolo ring substituted with R¹⁰, which rings can be fused to an R¹⁰-substituted benzene ring;
- 15 R⁵ is hydrogen; halogen; C₁ to C₁₂ alkyl; C₁ to C₁₂ haloalkyl; C₁ to C₁₂ alkoxy; C₃ to C₁₂ alkenyl; C₃ to C₁₂ haloalkenyl; C₃ to C₁₂ alkenyloxy; C₃ to C₁₂ alkynyl; C₃ to C₁₂ haloalkynyl; C₃ to C₁₂ alkylthio; C₁ to C₁₂ haloalkylthio; C₁ to C₁₂ haloalkoxy; C₁ to C₁₂ alkylsulfonyl; C₁ to C₁₂ haloalkylsulfonyl; nitro; phenyl substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; C₃ to C₁₂ alkynyoxy; C₂ to C₁₂ alkoxyalkyl; C₂ to C₁₂ alkoxyalkoxy; phenoxy methyl substituted on the phenyl ring with R⁶; phenethyloxy substituted on the phenyl ring with R⁶; phenethyl substituted on the phenyl ring with R⁶; benzyl substituted on the phenyl ring with R⁶; C₂ to C₁₂ carboalkoxy; C₅ to C₆ cycloalkyl; NMe₂; or NR⁸R⁹;
- 20 25 R⁶ is hydrogen; 1 to 2 halogen; C₁ to C₄ alkyl; trifluoromethyl; C₁ to C₄ alkoxy; methylthio; nitro; phenoxy; C₂ to C₆ cycloalkyloxy; or C₅ to C₆ cycloalkyl;
- R⁷ is hydrogen; or C₁ to C₄ alkyl;
- R⁸ is H; or C₁ to C₄ alkyl; R⁹ is H; phenyl substituted with H; 1-2 halogen; CF₃; C₁ to C₂ alkyl; or C₁ to C₂ alkoxy; and
- 30 R¹⁰ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;
- provided that, when A is oxygen, R³ is phenyl substituted with R⁵ and R⁶.
- Preferred for greatest fungicidal activity and/or ease of synthesis are:
- 35 2. The method of Preferred 1 wherein
- A is NR⁴;
- R¹ is C₁ to C₄ alkyl; C₁ to C₃ haloalkyl; vinyl; ethynyl; or methoxymethyl;
- R² is phenyl substituted with R⁵ and R⁶; C₅ to C₇ cycloalkyl; thienyl substituted with R⁶; or pyridyl substituted with R⁶;
- 40 R³ is phenyl substituted with R¹⁰; and
- R⁴ is H; C₁ to C₃ alkyl; or C₁ to C₃ alkylcarbonyl.
3. The method of Preferred 2 wherein
- R¹ is C₁ to C₄ alkyl or vinyl;
- R² is phenyl substituted with R⁵ and R⁶;
- 45 R³ is phenyl substituted with 1-2 halogen, methyl or methoxy;
- R⁴ is hydrogen or methyl;
- R⁵ is hydrogen; halogen; C₁ to C₄ alkyl; C₁ to C₄ haloalkyl; C₁ to C₆ alkoxy; benzyloxy; F₃CO; F₂HCO; C₁ to C₆ haloalkoxy; phenoxy substituted with R⁶; provided that if R⁵ is not H or F, then it is para to the point of attachment to the ring;
- 50 R⁶ is hydrogen, 1 to 2 F or Cl; methyl; or methoxy; and
- R⁷ is hydrogen.
4. The method of Preferred 3 wherein
- R¹ is CH₃;
- R⁴ is hydrogen or methyl;
- 55 R⁵ is H; F; Cl; CH₃; C₁ to C₆ alkoxy; or phenoxy substituted with halogen, CH₃, CH₃O or NO₂;
- R⁶ is H or F; and
- R¹⁰ is F; H or CH₃.
- Specifically preferred for greatest fungicidal activity and/or ease of synthesis are methods utilizing:

(1) 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.

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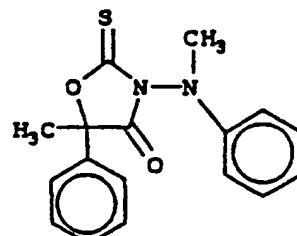
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(2) 5-methyl-5-phenyl-3-(N'-phenyl-N'-methylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.

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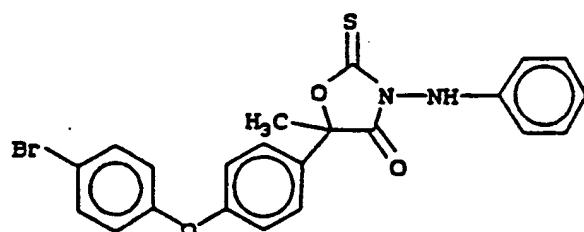


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(3) 5-[4-(4-bromophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.

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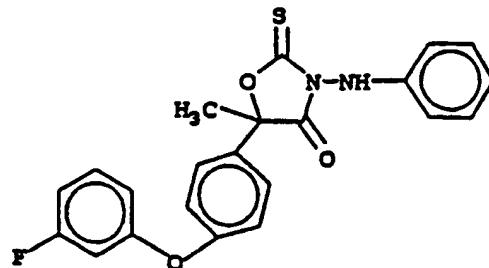
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(4) 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.

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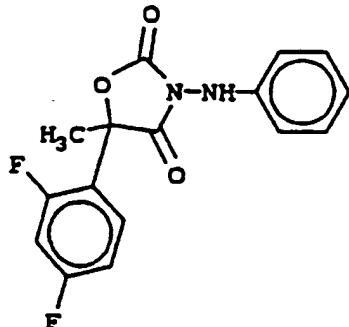
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(5) 5-(2,4-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer

thereof.

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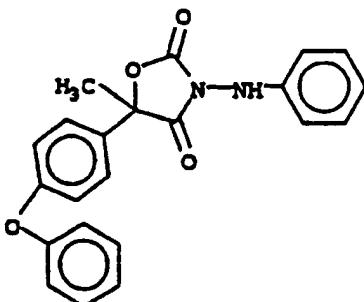


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(6) 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.

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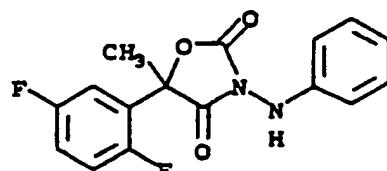
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(7) 5-(2,5-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.

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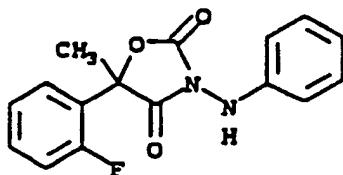
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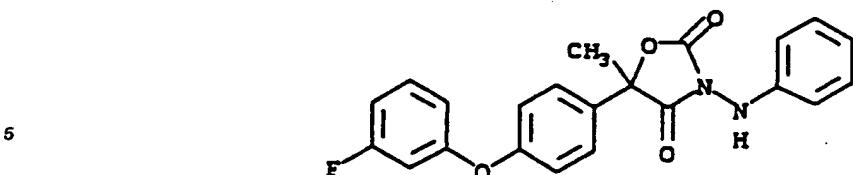
(8) 5-(2-fluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.

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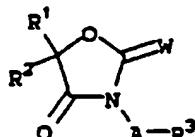
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(9) 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.



10 5. This invention also comprises novel compounds of Formula IA,

10



IA

20 wherein:

A is O or NR⁴;

W is O or S;

R¹ is H; C₁ to C₆ alkyl; C₁ to C₆ haloalkyl; C₃ to C₆ cycloalkyl; C₂ to C₆ alkenyl; C₂ to C₆ alkynyl; C₂ to C₆ alkoxyalkyl; C₁ to C₃ alkyl substituted with C₃ to C₆ cycloalkyl, phenyl or benzyl, wherein said phenyl or 25 benzyl ring is substituted on the ring with R⁶, and the benzylic carbon is substituted with R⁷;

R² is phenyl substituted with R⁵ and R⁶; naphthyl substituted with 1 to 2 groups selected from R⁵; thiienyl substituted with R⁵ and R⁶; furyl substituted with R⁶; pyridyl substituted with one of the following:

R⁶, phenoxy substituted with R⁶, or phenylthio substituted with R⁶;

30 C₁ to C₂ alkyl substituted with phenoxy or phenylthio, said phenoxy or phenylthio being substituted on the ring with R⁶;

C₁ to C₆ alkyl; or

C₅ to C₇ cycloalkyl; and

35 R¹ and R² can be taken together, along with the carbon to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5 to 7 ring atoms in which the heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; and the carbocyclic ring can be fused with 1 or 2 R⁵-substituted benzene rings or with an R⁶-substituted thiophene ring;

40 R³ is phenyl substituted with R¹⁰; benzyl substituted on the benzylic carbon with a group selected from R⁷ and substituted on the phenyl ring with R¹⁰; naphthyl substituted with R¹⁰; additionally, R³ can be thiienyl substituted with R¹⁰, furyl substituted with R¹⁰, pyridyl substituted with R¹⁰, pyrimidyl substituted with R¹⁰, or pyridazyl substituted with R¹⁰; or R³ can be C₂ to C₁₀ alkyl or C₅ to C₇ cycloalkyl;

45 R⁴ is hydrogen; formyl; C₂ to C₄ alkylcarbonyl; C₂ to C₄ haloalkylcarbonyl; C₂ to C₄ alkoxyalkylcarbonyl; C₂ to C₄ alkoxy carbonyl; C₂ to C₅ alkylaminocarbonyl; C₁ to C₄ alkylsulfonyl; C₁ to C₄ alkyl; C₄ to C₆ cycloalkyl; phenylaminocarbonyl where said phenyl is substituted with R¹⁰; and R⁴ can be C₃ to C₄ alkenyl or C₃ to C₄ alkynyl; or

50 R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a pyrrolidino, piperidino or pyrrolo ring substituted with R¹⁰, which rings can be fused to an R¹⁰-substituted benzene ring;

55 R⁵ is hydrogen; halogen; C₁ to C₁₂ alkyl; C₁ to C₁₂ haloalkyl; C₁ to C₁₂ alkoxy; C₃ to C₁₂ alkenyl; C₃ to C₁₂ haloalkenyl; C₃ to C₁₂ alkenyloxy; C₃ to C₁₂ alkynyl; C₃ to C₁₂ haloalkynyl; C₃ to C₁₂ alkylthio; C₁ to C₁₂ haloalkylthio; C₁ to C₁₂ haloalkoxy; C₁ to C₁₂ alkylsulfonyl; C₁ to C₁₂ haloalkylsulfonyl; nitro; phenyl substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; C₃ to C₁₂ alkynyoxy; C₂ to C₁₂ alkoxyalkyl; C₂ to C₁₂ alkoxyalkoxy; phenoxy methyl substituted on the phenyl ring with R⁶; benzyl oxy substituted on the phenyl ring with R⁶; phenethyloxy substituted on the phenyl ring with R⁶; phenethyl substituted on the phenyl ring with R⁶; benzyl substituted on the phenyl ring with R⁶; C₂ to C₁₂ carboalkoxy; C₅ to C₆ cycloalkyl; NMe₂; or NR⁸R⁹;

60 R⁶ is hydrogen; 1 to 2 halogen; C₁ to C₄ alkyl; trifluoromethyl; C₁ to C₄ alkoxy; methylthio; nitro; phenoxy; C₂ to C₆ cycloalkyloxy; or C₅ to C₆ cycloalkyl;

R⁷ is hydrogen; or C₁ to C₄ alkyl;

R⁸ is H; or C₁ to C₄ alkyl;

R⁹ is H; phenyl substituted with H; 1-2 halogen; CF₃; C₁ to C₂ alkyl; or C₁ to C₂ alkoxy; and

R¹⁰ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or

- 5 CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;

provided that

(1) when A is O, then R³ is phenyl substituted with R⁵ or R⁶;

(2) when R² is unsubstituted phenyl, then R¹ is not hydrogen, methyl or benzyl;

- 10 (3) when R¹ is hydrogen, methyl or cyclohexyl, then R² is not methyl, isopropyl or cyclohexyl; and

(4) R¹ and R² do not join to form -(CH₂)₅-.

Preferred for greatest fungicidal activity and/or ease of synthesis are:

6. A compound of Formula IA wherein

A is NR⁴;

- 15 R¹ is C₁ to C₄ alkyl; C₁ to C₃ haloalkyl; vinyl; ethynyl; or methoxymethyl;

R² is phenyl substituted with R⁵ and R⁶; C₅ to C₇ cycloalkyl; thiaryl substituted with R⁶; or pyridyl substituted with R⁶;

R³ is phenyl substituted with R¹⁰; and

R⁴ is H; C₁ to C₃ alkyl; or C₁ to C₃ alkylcarbonyl;

- 20 provided that when R² is unsubstituted phenyl, R¹ is not methyl.

7. A compound of Formula IA wherein

R¹ is C₁ to C₄ alkyl or vinyl;

R² is phenyl substituted with R⁵ and R⁶;

R³ is phenyl substituted with 1-2 halogen, methyl or methoxy;

- 25 R⁴ is hydrogen or methyl;

R⁵ is hydrogen; halogen; C₁ to C₄ alkyl; C₁ to C₄ haloalkyl; C₁ to C₆ alkoxy; benzyloxy; F₃CO; F₂HCO; C₁ to C₆ haloalkoxy; phenoxy substituted with R⁶; provided that if R⁵ is not H or F, then it is para to the point of attachment to the ring;

R⁶ is hydrogen, 1 to 2 F or Cl; methyl; or methoxy; and

- 30 R⁷ is hydrogen;

provided that when R² is unsubstituted phenyl, R¹ is not methyl.

8. A compound of Formula IA wherein

R¹ is CH₃;

R⁴ is hydrogen or methyl;

- 35 R⁵ is H; F; Cl; CH₃; C₁ to C₆ alkoxy; or phenoxy substituted with halogen, CH₃, CH₃O or NO₂;

R⁶ is H or F; and

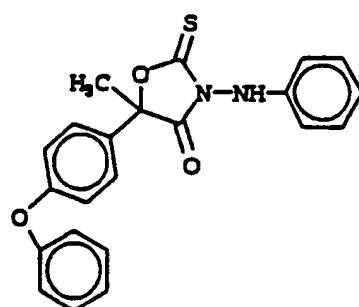
R¹⁰ is F; H or CH₃;

provided that R² is not unsubstituted phenyl.

- Specifically preferred for greatest fungicidal activity and/or ease of synthesis are the following
40 compounds:

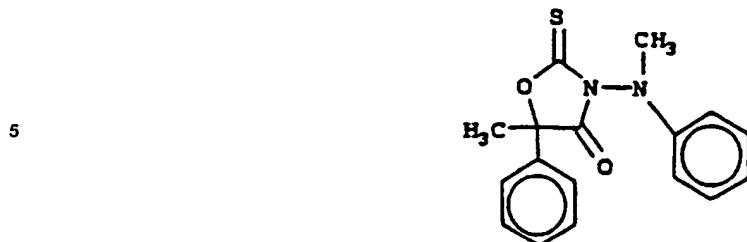
(1) 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.

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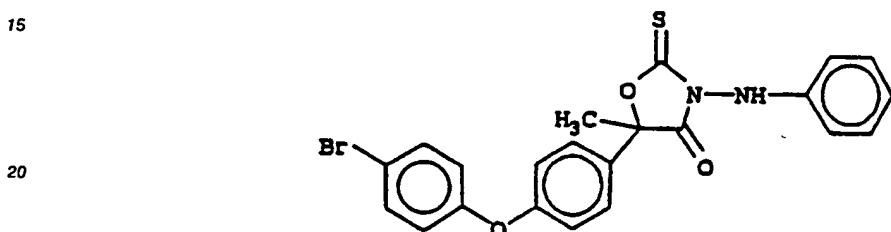


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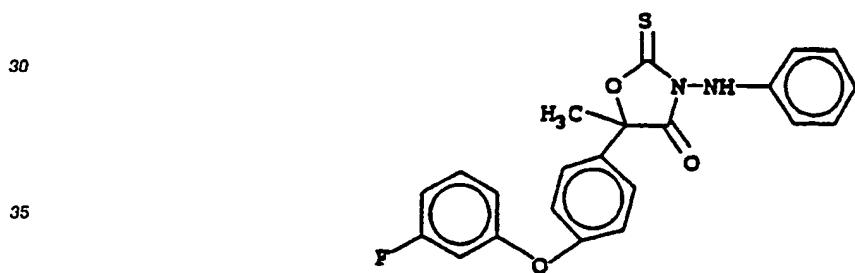
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(2) 5-methyl-5-phenyl-3-(N'-phenyl-N'-methylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.



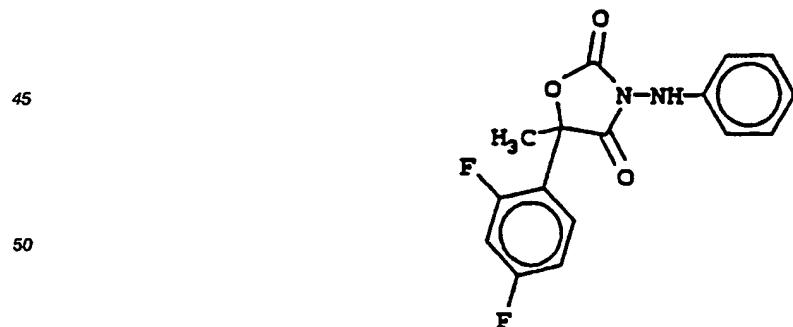
(3) 5-(4-(4-bromophenoxy)phenyl)-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.



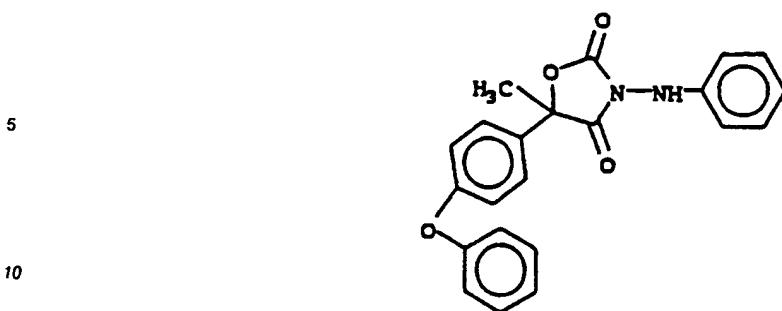
25 (4) 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof.



40 (5) 5-(2,4-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.



55 (6) 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof.



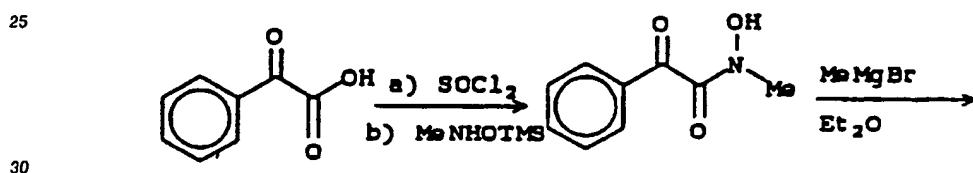
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DETAILED DESCRIPTION OF THE INVENTION

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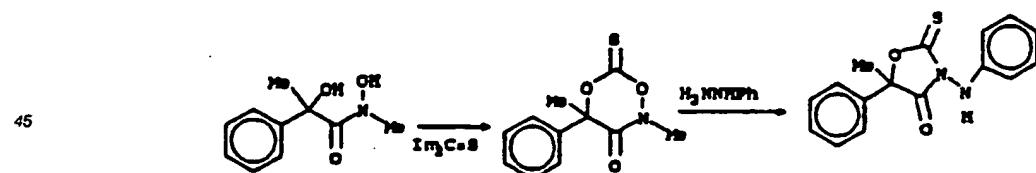
Synthesis

The compounds of this invention may be prepared by the route outlined below to 5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone:



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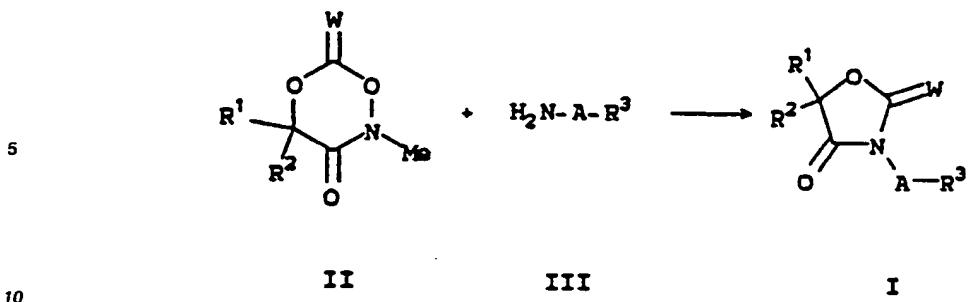


50 Details of these procedures and related variations are described in the following Equations.

One skilled in the art will recognize that when R¹ and R² are different, compounds of Formula I in Equation 1 possess a chiral center. This invention pertains to racemic mixtures and to pure enantiomers. Although one enantiomer may have superior fungicidal activity for a given compound of Formula I, the other enantiomer is not devoid of activity nor does it interfere with the activity of the more potent enantiomer.

55 As shown in Equation 1, compounds of Formula I can be prepared by treating heterocycles of type II with an appropriate amine III.

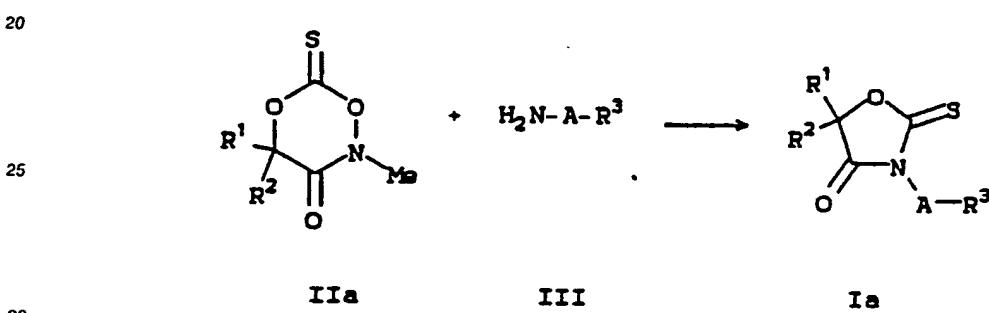
Equation 1



The reactions are conducted at 0 °C to 50 °C in an inert solvent such as methylene chloride, THF, or benzene. Detailed experimental procedures are disclosed in the references cited below.

15 Compounds described by Formula I wherein W is S can be prepared as illustrated in Equation 2.

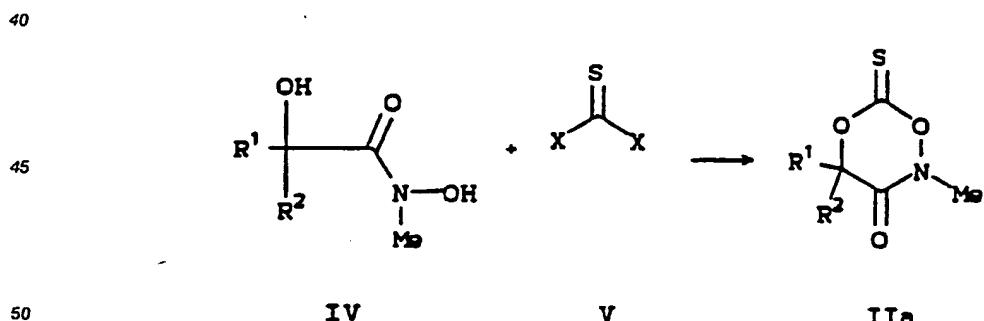
Equation 2



Treatment of thioxodioxazinones IIa with hydroxylamines (A=O) or hydrazines (A=NR⁴) in an inert solvent such as methylene chloride, benzene, or THF at temperatures ranging from -10 °C to 35 °C gives the thioxooxazolidinones Ia. [Geffken, D.; *Z. Naturforsch.*, 1983, 38b, 1008]

35 The thioxodioxazinones IIa are prepared according to the method outlined in Equation 3.

Equation 3



55 The hydroxamic acids IV are reacted with a thionoating agent V, such as thiophosgene (X=Cl) in the presence of a base or 1,1'-thiocarbonyldiimidazole (X=imidazole), to afford the thioxodioxazinones IIa. The reactions are performed at -20 °C to 25 °C in an inert solvent. [Geffken, D., *Z. Naturforsch.*, 1983, 38b, 1008] The products are generally unstable at ambient temperature and therefore are reacted with the desired amine III immediately upon isolation.

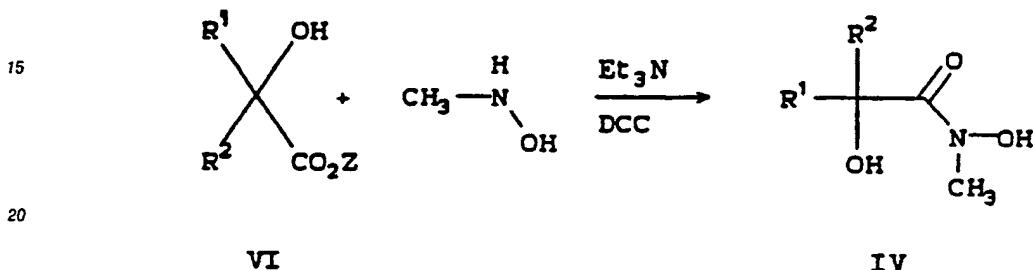
Preparation of the hydroxylamines [Castellino, A. J.; Rapoport, H.; *J. Org. Chem.*, 1984, 49, 1348] (III,

A = O) and hydrazines [J. Timberlake; J. Stowell; *The Chemistry of the Hydrazo, Azo, and Azoxy Groups* (S. Patai, Ed.) John Wiley and Sons, Ltd., London (1975), p. 69; Demers, J. P.; Klaubert, D. J.; *Tetrahedron Lett.*, 1987, 4933] (III, A = NR⁴) can be accomplished by literature methods by one skilled in the art.

- The synthesis of the requisite hydroxamic acids IV can be accomplished by several known methods. As shown in Equation 4, the condensation of an α -hydroxycarboxylic acid VI ($Z=H$) with N-methylhydroxylamine hydrochloride affords the desired hydroxamic acids IV. [Geffken, D.; Kampf, H.; J. Chem. Ztg., 1979, 103, 19] Triethylamine is commonly used as an added base and 1,3-dicyclohexylcarbodiimide (DCC) is used as the dehydrating agent.

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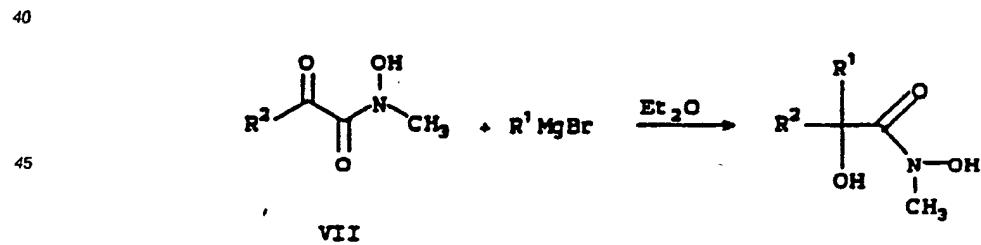
Equation 4



25 2-Hydroxycarboxylic acids can be purchased from commercial sources, or generally prepared from ketones or aldehydes by formation of cyanohydrins, then hydrolysis, as is known in the art. For example, Org. Syn. Coll. Vol. IV, 58 (1968) teaches the preparation of atrolactic acid from acetophenone. Esters can be prepared from the 2-hydroxycarboxylic acids by methods known in the art. Alternatively, aryl α -hydroxycarboxylic acid esters can also be prepared by treating pyruvate esters with nucleophilic organometallic reagents such as phenyl magnesium bromide or phenyl lithium as described in the literature (Salomon, R. G., Pardo, S. N., Ghosh, S., J. Org. Chem., 1982, 47, 4692). The "Dictionary of Organic Compounds", Vol. 3, 4th ed. (1965), page 1791 (Oxford Univ. Press) lists atrolactic acid and esters.

Alternative methods for producing compounds of Formula IV are known in the literature. As illustrated in Equation 5, α -hydroxyhydroxamic acids IV can also be synthesized by treating α -ketohydroxamic acids VII with an excess of a Grignard reagent. [Geffken, D.; Burchardt, A.; Arch. Pharm., 1988, 321, 311] The reactions are conducted in refluxing ether for 2 to 6 hours.

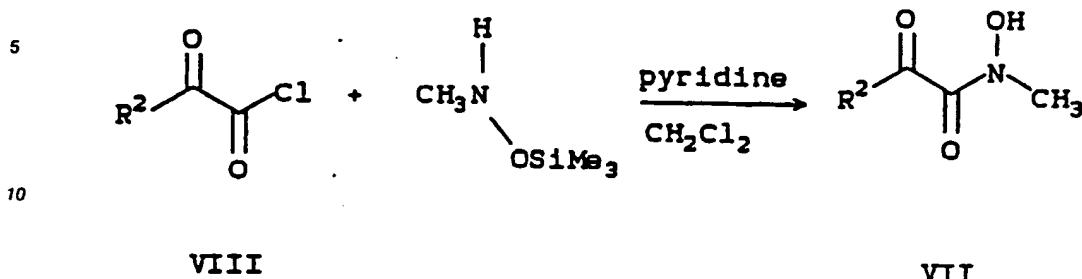
Equation 5



This procedure works best in cases where R² of the hydroxamic acids VII is a non-enolizable group, for

The α -ketohydroxamic acids VII can be prepared by condensing the glyoxylic acid chlorides VIII, derived from the corresponding carboxylic acids, [Geffken, D.; Burchardt, A.; Arch. Pham., 1988, 321, 311] with O-trimethylsilyl-N-methylhydroxylamine [Geffken, D.; Burchardt, A.; Arch. Pham., 1988, 321, 311] (Equation 6).

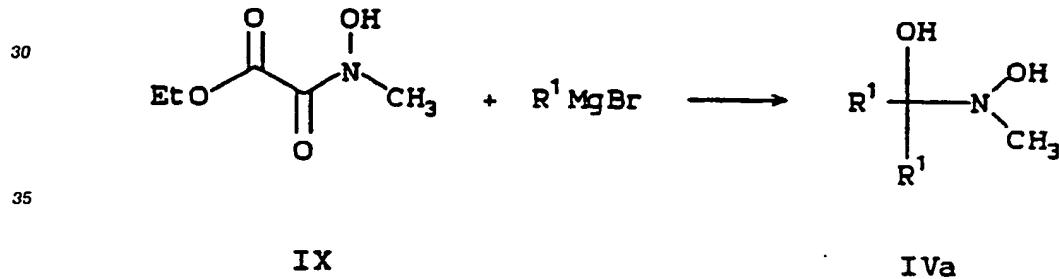
Equation 6



15 These reactions are conducted in a mixture of pyridine and methylene chloride at 0° C to 25° C.
 The starting α -ketoacids VIII are either purchased from commercial sources or obtained by oxidation of the corresponding methyl ketone with selenium dioxide. [Hallmann, G.; Haegele, K.; Annalen, 1963, 662, 147]

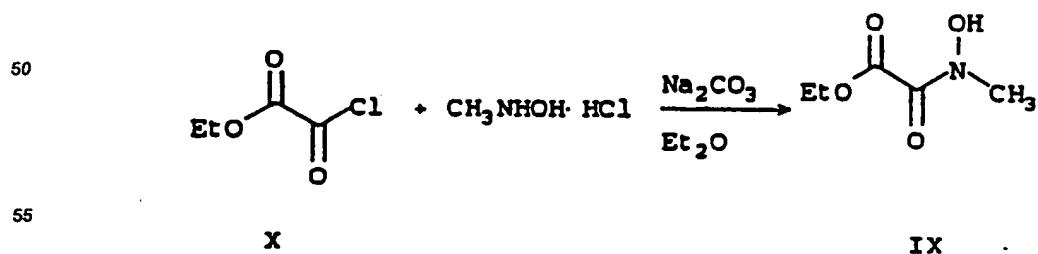
20 A third method for producing α -hydroxyhydroxamic acids IV is specific to examples in which $R^1 = R^2$ (IVa). This method, illustrated in Equation 7, involves adding an excess of Grignard reagent, typically five equivalents, to a solution of the hydroxamic acids IX in ether. [Geffken, D., Arch. Pharm., 1987, 320, 382]. The reactions are normally performed at reflux.

25 Equation 7



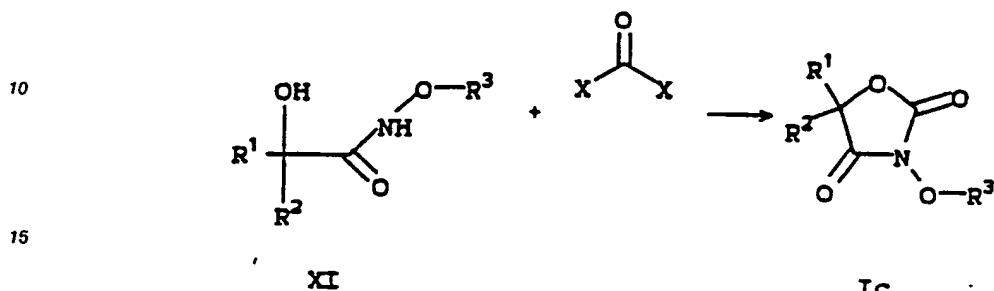
⁴⁰ The starting hydroxamic acids IX are prepared by treating ethyl oxalyl chloride X with N-methylhydroxylamine hydrochloride. Sodium carbonate is added as an acid scavenger (Equation 8). [Geffken, D., Arch. Pharm., 1987, 320, 382]

45 Equation 8



Compounds of general Formula I wherein W and A are O (Ic) are prepared by the methods shown in Equation 9.

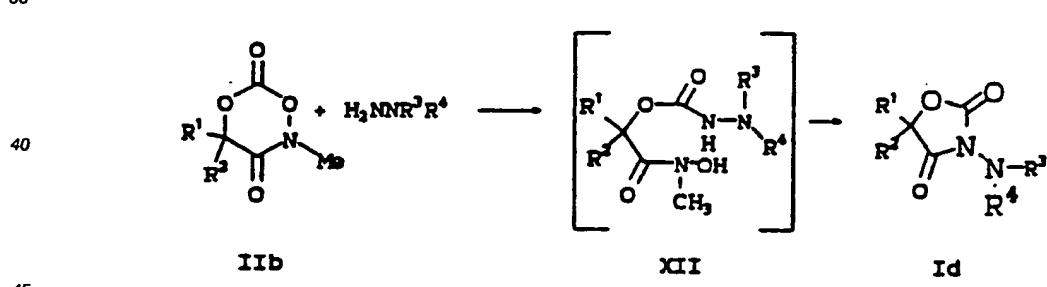
5 Equation 9



20 The addition of a carbonylating agent, e.g. phosgene ($X=Cl$), 1,1'-thiocarbonyldiimidazole ($X=imidazole$), or oxalyl chloride, to hydroxamic acids of type XI produces dioxotetrahydrooxazoles Ic. The cyclizations can be conducted in an inert solvent, for example benzene or methylene chloride, at temperatures ranging from 0 °C to 80 °C. Experimental details for reactions of this type have been reported as have the preparation of the starting hydroxamic acids XI. [Geffken, D.; Zinner, G.; Chem. Ber., 1973, 106, 2246]

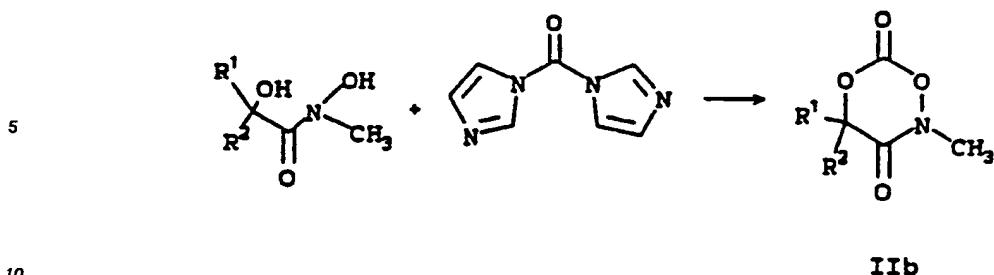
25 Compounds of Formula I in which W is O and A is NR⁴ (Id) are synthesized by treating hydroxamic acids IIb with various hydrazines, as illustrated in Equation 10. Depending on the nature of the substituents on IIb and the reacting hydrazine, the intermediate N-aminocarbamates XII may or may not be isolated. For cases in which ring closure is not spontaneous under the reaction conditions, treatment of XII with triethylamine in an inert solvent (such as THF) at temperatures ranging from 25 °C to 80 °C induces cyclization to Id. [Geffken, D.; Arch. Pharm., 1982, 315, 802; Geffken, D., Synthesis, 1981, 38]

35 Equation 10



40 The dioxazinediones IIb are readily prepared from the corresponding α-hydroxyhydroxamic acid by treatment with 1,1'-carbonyldiimidazole (Equation 11). The cyclization is performed in an inert solvent such as methylene chloride and is complete in less than one minute at 25 °C. [Geffken, D.; Arch. Pharm., 1982, 315, 802; Geffken, D., Synthesis, 1981, 38]

45 Equation 11



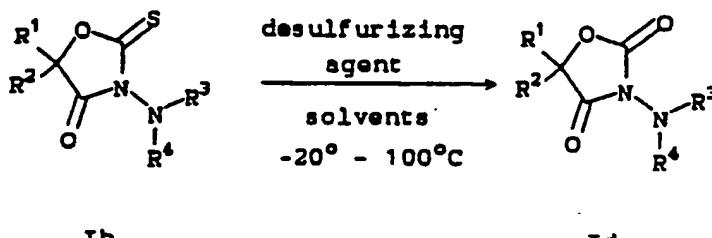
In addition to the methods described above, oxazolidinediones described by Formula I wherein W is O can be prepared by desulfurization of thioxooxazolidinones as shown in Equation 12.

15

Equation 12

20

25



30 A general procedure for preparing the oxazolidinediones is described below. The thioxooxazolidinone (Ib) is dissolved in a water-miscible organic solvent such as methanol, acetone, acetonitrile, dimethylformamide, dioxane, tetrahydrofuran, etc. Methanol and acetone are preferred. The solution is treated with a desulfurizing agent such as aqueous OZONE® (KHSO₅), aqueous silver nitrate, bleach (NaOCl), various peroxides and peracids or other reagents known by those skilled in the art to oxidize sulfur. Aqueous OZONE® and aqueous silver nitrate are preferred. The reaction mixture is stirred at temperatures ranging from about -20 °C to about 100 °C until the reaction is complete.

35 The product can be isolated by evaporation of the solvent, and purified by washing with water in a water-immiscible solvent such as methylene chloride or ether. Drying, evaporation of the solvent, followed by further purification by recrystallization or chromatography affords pure oxazolidinediones, Id.

40 A novel process for preparing thioxooxazolidinones Ib expeditiously and in good yield is also disclosed herein. The process comprises four sequential reactions:

- (1) reaction of a 2-hydroxycarboxylic acid ester with a base;
- (2) reaction of the product of reaction (1) with carbon disulfide;
- (3) reaction of the product of reaction (2) with an acylating agent; and
- 45 (4) reaction of the product of reaction (3) with a substituted hydrazine.

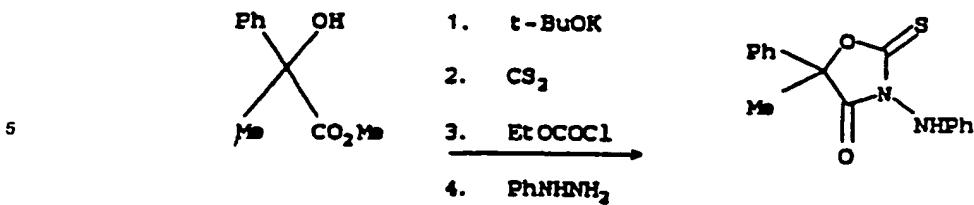
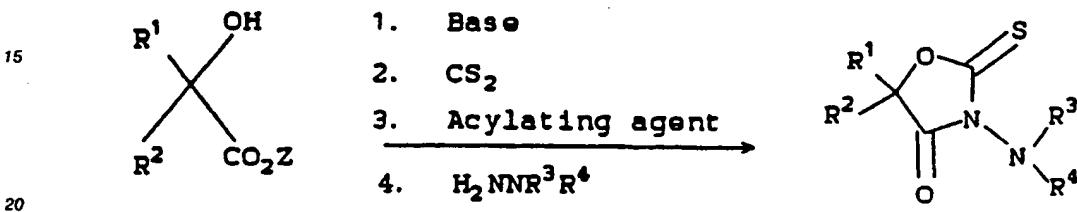
This sequence of reactions can be conveniently conducted in a single reaction vessel without isolation of chemical intermediates.

The process is represented in Equation 13 for the specific case of preparation of 5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone, and in Equation 14 for the general case:

50

Equation 13

55

Equation 14

25 The preparation of the α -hydroxyesters VI in Equation 14 is discussed above. The ester group can be alkyl ($\text{C}_1\text{-C}_{12}$), alkenyl ($\text{C}_3\text{-C}_4$), cycloalkyl ($\text{C}_3\text{-C}_{12}$), cycloalkylalkyl ($\text{C}_6\text{-C}_7$), alkoxyalkyl ($\text{C}_2\text{-C}_4$) or benzyl. Preferred for ease of synthesis, lower expense or greater utility are esters in which Z is $\text{C}_1\text{-C}_4$ alkyl.

30 Thioxooxazolidinones Ib prepared by this method preferred for reasons of ease of synthesis, lower expense or greater utility, are compounds wherein:

R^1 is methyl;

R^2 is phenyl substituted with R^5 and R^6 ;

R^3 is phenyl substituted with R^{10} ; and

R^4 is hydrogen.

35 In each of the reaction steps of Equation 14 it will be understood by those skilled in the art that the optimum combination of reaction time, reaction temperature, stoichiometry, solvent(s), and the like will depend on the exact product being prepared, as well as on the relative importance of these factors and the results to the individual operator. For example:

40 The reaction time should be sufficient to effect the desired reaction; the reaction temperature should be sufficient to effect the desired reaction in the desired time without undue decomposition or side reactions; the stoichiometry of reactants should generally be the theoretical values, in the interest of economy, with variations as needed to compensate for evaporative or other losses; and solvent(s) can be selected, e.g., so that reaction ingredients have a substantial solubility, in the interest of obtaining relatively fast reaction rates.

45 In Reaction Step 1 - Usable bases are those capable of deprotonation of the hydroxy group without unacceptable side reactions. Included are the alkali metal tertiary alkoxides, hydrides, and hydroxides. Preferred among these in the interest of higher solubility, reactivity, ease or safety of use, higher yields, or economy are the potassium tertiary alkoxides such as potassium tert.-butoxide and potassium tert.-amylate. Especially preferred is potassium tert.-butoxide.

50 Usable solvents are the 2-hydroxycarboxylic acid ester itself and generally the non-hydroxylic solvents, including ethers (e.g. diethyl ether, tetrahydrofuran, dioxane, 1,2-dimethoxyethane), esters (e.g. methyl and ethyl acetate), amides (e.g. N,N-dimethylformamide, N,N-dimethylacetamide, 1-methyl-2-pyrrolidone), nitriles (e.g. acetonitrile), and the like, and mixtures containing one or more of these solvents. Preferred among these solvents are those in which the reactants have substantial solubility.

55 The temperature can vary from about -80°C to about $+100^\circ\text{C}$, with about -20°C to $+80^\circ\text{C}$ preferred, and with about -5°C to $+50^\circ\text{C}$ more preferred. Ambient temperature is a convenient temperature at which to conduct the reaction.

The needed reaction time is short with soluble reactants. No more than a few minutes are required at

ice to ambient temperatures, e.g. 0.5 to 15 minutes.

In Reaction Step 2, carbon disulfide (CS₂) is contacted with the product of Step 1 at about -20 °C to +100 °C, preferably -10 °C to +50 °C, for about 5 seconds to about 24 hrs., preferably for about 5 to 30 min. The reaction is rapid for soluble reactants. Ambient temperature is a convenient temperature at which to conduct the reaction.

- 5 In Reaction Step 3 an acylating agent capable of forming a mixed-anhydride with the product of Reaction Step 2 is contacted with the product of Reaction Step 2. Such acylating agents include chloroformates, e.g. methyl chloroformate, ethyl chloroformate, propyl chloroformate, butyl chloroformate, and benzyl chloroformate, and other acylating agents. Preferred acylating agents are methyl and ethyl chloroformate. The reaction is rapid, and is complete in about 5 seconds to an hour with soluble reactants.
- 10 Most reactions are complete in about 1 to 30 minutes. The temperature can range from about -20 °C to +50 °C. The preferred range is from about -10 °C to +25 °C. Ice to ambient temperatures is a convenient temperature range for conducting this reaction.

- 15 In Reaction Step 4 the substituted hydrazine reactant is contacted with the product of Reaction Step 3. The substituted hydrazine can be used as the free base or as a mixture of its acid salt with an added acid scavenger such as a tertiary amine base (e.g. triethylamine, N,N-diisopropyl-N-ethylamine). The reaction is rapid, requiring no more than a few minutes for completion with soluble reactants. Reaction times may be 10 seconds to about 1 day, preferably about 1 minute to 8 hrs. Reaction temperatures can range from about -20 °C to +100 °C. Ice to ambient temperatures is a convenient range at which to conduct the reaction.
- 20 The product of Step 4 can be isolated by evaporation of the reaction solvent, and it can be purified if desired by dissolving in a water-immiscible solvent (e.g. carbon tetrachloride, butyl chloride, ether), washing with water, mineral acid, and base, followed by drying and evaporation of solvent, in turn followed by crystallization or chromatography as desired.
- 25 The compounds that can be made by the process of this invention are described in the Examples and Tables which follow, and are intended to be only exemplary and not all-inclusive.

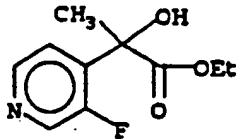
EXAMPLE 1

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Ethyl 2-(3-fluoropyrid-4-yl)lactate

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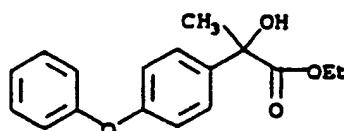
A 27 mL portion of commercially-available 2.03 M lithium diisopropylamide-THF/heptane solution (Lithco) was diluted with 50 mL of dry THF, cooled to -60 °C under nitrogen, and stirred while adding a solution of 4.3 mL (4.8 g, 50 mmol) of 3-fluoro pyridine in 10 mL of dry THF at a rate that held the mixture below -55 °C. The resulting slurry was stirred at -60 °C for another 30 minutes, and then with continued cooling and stirring a solution of 6.0 mL (6.4 g, 55 mmol) of ethyl pyruvate in 30 mL of dry THF was added as quickly as possible while maintaining an internal temperature of -60 °C. The resulting thin slurry was allowed to come to -10 °C, then diluted with 200 mL each of water and ether. The aqueous phase was adjusted to pH 7 by addition of 1N aqueous HCl, the ether phase was separated, the aqueous phase was extracted with two 100 mL portions of ether, and the combined ether phases were washed with three 100-mL portions of water and 100 mL of brine, dried over magnesium sulfate, and evaporated to leave 5.8 g of a dark brown oil. Chromatography over silica gel, eluting with methylene chloride-methanol 99:1, provided 3.7 g (35%) of the title compound as a pale yellow solid: mp 56-60 °C; IR (Nujol) 2600-3400, 1755, 1730 cm⁻¹; NMR (CDCl₃, 200 MHz) 1.2 (3H, t, J=7), 1.8 (3H, s), 3.9 (1H, s), 4.3 (2H, q, J=7), 7.5 (1H, d of d, J=5,7), 8.4-8.5 (2H, m).

EXAMPLE 2

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Ethyl 2-(4-phenoxyphenyl)lactate

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A 250-mL flask fitted with magnetic stirring, water condenser, 125 mL dropping funnel, thermometer, and nitrogen inlet was charged with 2.7 g (110 mmol) of magnesium metal and dried with a heat gun under strong nitrogen purge. After cooling, the funnel was charged with a solution of 17.5 mL (24.9 g, 100 mmol) of 4-bromodiphenyl ether in 67 mL of dry THF, and 10 mL was run into the flask. With stirring, the Grignard initiated spontaneously, and the rest of the bromide solution was added over 15 minutes, maintaining an internal temperature of 67-68 °C. When addition was complete, the temperature held at 68 °C for 5 minutes, then began to drop, reaching 30 °C after 45 minutes.

Meanwhile, a 250 mL flask, magnetic stirrer, and 125 mL dropping funnel that had been oven-dried were assembled hot under nitrogen and allowed to cool. A low-temperature thermometer was then added, the flask was charged with a solution of 11.5 mL (12.2 g, 105 mmol) of ethyl pyruvate in 66 mL of dry THF, and the solution of Grignard reagent was transferred to the dropping funnel by means of a syringe. The pyruvate solution was chilled to -10 °C, and the Grignard solution was run in over 15 minutes with good stirring, cooling to maintain an internal temperature of -5 to -10 °C.

The resulting solution was stirred and treated with 50 mL of water followed by 50 mL of saturated aqueous ammonium chloride, giving two clear phases. These were separated, and the upper phase was subjected to rotary evaporation to remove most of the THF. Addition of 50-mL portions of water and methylene chloride gave two clear phases.

These were separated, the aqueous phase was washed with another 25 mL of methylene chloride, and the combined organic phases were washed with water and brine, dried over magnesium sulfate, and evaporated to leave 23.8 g of yellow-orange oil. Kugelrohr distillation at 140 °C/0.1-0.2 mm for 60 minutes removed volatile impurities, leaving 17.1 g (60%) of the product as a clear orange oil: n_{D}^{26} 1.5555; IR (neat) 3490, 1725 cm^{-1} ; NMR (CDCl_3 , 200 MHz) 1.3 (3H, t, $J=7$), 1.8 (3H, s), 3.8 (1H, broad s), 4.2 (2H, m), 6.9-7.0 (4H, m), 7.1 (1H, t, $J=7$), 7.3 (2H, t, $J=7$), 7.5 (2H, d, $J=9$).

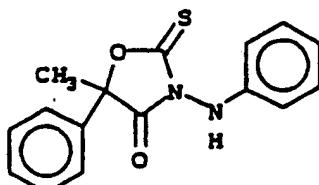
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EXAMPLE 3

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Preparation of 5-Methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone

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A solution of methyl atrolactate (7.64 g, 0.0424 mole) in tetrahydrofuran (80 ml) was stirred and cooled in an ice bath, and potassium tert.-butoxide (4.76 g, 0.0424 mole) was added. The ice bath was removed,

and the mixture was stirred for 10 minutes. This procedure provided a clear, yellow solution at 21°C.

Carbon disulfide (2.8 ml, 0.046 mole) was added, and caused the formation of an orange color and a temperature rise to 32°C. The solution was cooled in an ice bath for 10 minutes, causing the temperature to fall to 4°C.

5 Ethyl chloroformate (4.1 ml, 0.043 mole) was added to the ice-cooled solution, inducing the formation of a turbid yellow mixture and a temperature rise to 12°C. The mixture was stirred with ice-bath cooling for 5 minutes as the temperature fell to 5°C.

10 Phenylhydrazine (97%, 4.5 ml, 0.044 mole) was added. The temperature rose to 24°C while the cooling bath was applied. After the temperature fell to 20°C, the mixture was stirred for 10 minutes, then 15 evaporated under reduced pressure to an oil.

The oil was mixed with 1-chlorobutane and water, and the layers were separated. The organic layer was washed with 1N HCl, water, and saturated aq. sodium bicarbonate solution. The organic solution was dried (magnesium sulfate), filtered, and evaporated under reduced pressure to an oil. The oil was crystallized from carbon tetrachloride/hexane (~40 ml/20 ml), providing the product (7.40 g, 58.5% of theory) as a light-yellow solid, m.p. 104-105°C. The product was further purified by recrystallization from carbon tetrachloride/hexane with 93% recovery.

In another preparation of the same product, carbon tetrachloride was used instead of 1-chlorobutane during the workup. Crystallization from the carbon tetrachloride solution by dilution with hexane provided the product in 54% yield. Recrystallization from isopropanol/water provided the product as a white solid, m.p. 20 108-109°C, with 92% recovery.

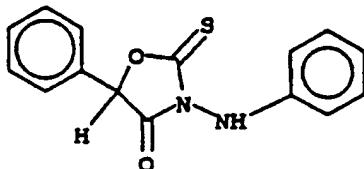
EXAMPLE 4

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Preparation of 5-Phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone

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35



A stirred solution of potassium tert-butoxide (11.22 g, 0.1 mole) in tetrahydrofuran (100 ml), held at 40 0°C to -5°C, was treated portionwise with a solution of methyl mandelate (16.62 g, 0.1 mole) in tetrahydrofuran (70 ml), providing an orange-red solution. After 4 minutes carbon disulfide (6.04 ml, 0.1 mole) was added. After 5 minutes at 0°C to -5°C, the orange solution was cooled to -30°C and treated with ethyl chloroformate (9.5 ml, 0.1 mole). After 2 minutes the solution was warmed to -10°C. After 5 minutes at -10°C, the solution was cooled to -30°C and treated with 97% phenylhydrazine (10.1 ml, 0.1 mole). The yellow solution was warmed to 25°C, and after 10 minutes the mixture was evaporated under reduced pressure to a turbid oil. The oil was mixed with water and 1-chlorobutane, the layers were separated, and the organic solution was washed with 1N HCl, water (twice), and saturated sodium bicarbonate solution. The dried (magnesium sulfate) solution was evaporated under reduced pressure to a yellow-orange oil, and the oil was dissolved in chloroform. A silica-gel filtration of the chloroform solution followed by evaporation of the filtrate under reduced pressure provided a green oil which began to solidify. Further purification was accomplished by crystallization from 1-chlorobutane. This procedure provided the product as 9.9 g (35% of theoretical) of a white solid, m.p. 140-141°C. The infrared spectrum (Nujol mull) showed the characteristic absorption at 3295 cm⁻¹ (N-H) and 1760 cm⁻¹ (imide C=O).

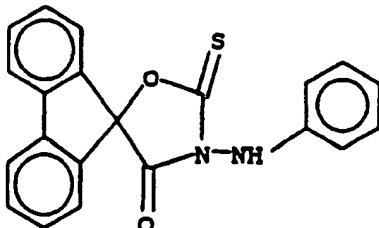
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EXAMPLE 5

Preparation of 3'-(Phenylamino)-2'-thioxo-spiro(9H-fluorene-9,5'-oxazolidin)-4'-one

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15 A solution of 9-hydroxy-9-fluorenecarboxylic acid, methyl ester (8.91 g, 0.0371 mole) in tetrahydrofuran (89 ml) was treated with potassium tert-butoxide (4.16 g, 0.0371 mole). After 6 minutes the solution was cooled in an ice bath and carbon disulfide (2.3 ml, 0.038 mole) was added. After 7 minutes ethyl chloroformate (3.6 ml, 0.038 mole) was added to the cold solution. After 7 minutes 97% phenylhydrazine (3.9 ml, 0.038 mole) was added. After 3 minutes, the mixture was evaporated under reduced pressure to a yellow syrup. The syrup was treated with 1-chlorobutane and water, and the organic layer was washed with saturated sodium bicarbonate solution, water, 1N HCl, and water. The dried (magnesium sulfate) solution was filtered and evaporated under reduced pressure to an oil. The oil was crystallized from carbon tetrachloride/hexane, and the solid product further purified by boiling with isopropanol (without dissolution of all solid), cooling, and filtering. The product was obtained as 3.56 g (27% of theoretical) of analytically-pure white solid, m.p. 187-189 °C.

20 Anal. Calcd. for $C_{21}H_{14}N_2O_2S$: C, 70.37; H, 3.94; N, 7.82%. Anal. Found: C, 70.28; H, 4.19; N, 7.68%.
 The infrared spectrum (Nujol mull) showed absorption at 3275 cm^{-1} (N-H) and 1770 cm^{-1} (imide C=O).

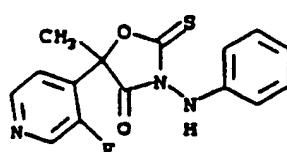
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EXAMPLE 6

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5-(3-Fluoropyrid-4-yl)-5-methyl-3-phenylamino-2-thioxo-4-oxazolidinone

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45 A solution of 3.2 g (15 mmol) of ethyl 2-(3-fluoropyrid-4-yl)lactate in 20 mL of THF was stirred and chilled in an ice-water bath while 1.6 g (15 mmol) of solid potassium tertiary-butoxide was added in portions. The cooling bath was then removed, 1.0 mL (1.2 g, 15.5 mmol) of carbon disulfide was added, the mixture was stirred for 10 minutes, cooling was resumed, 1.4 mL (1.6 g, 15 mmol) of ethyl chloroformate was added, the mixture was stirred for 10 minutes, 1.5 mL (15 mmol) of phenylhydrazine was added, the resulting slurry was stirred and allowed to come to room temperature, another 20 mL of THF was added, and the mixture was stirred another 15 minutes at room temperature. Most of the solvent was then removed by rotary evaporation, the residue was partitioned between 1-chlorobutane and water, and the organic phase was separated, washed with 0.1N aqueous HCl, water, saturated aqueous sodium bicarbonate, water, and brine, dried over magnesium sulfate, and evaporated to leave 3.7 g of a green gum. Chromatography over silica gel, eluting with methylene chloride:methanol 98:2, provided 1.7 g (35%) of the title compound as a semisolid. Crystallization from ethyl acetate-hexanes 1:1 gave pale yellow crystals: mp 165-169 °C; IR (Nujol) 3200, 3130, 1780 cm^{-1} ; NMR ($CDCl_3$, 200 MHz) 2.2 (3H, s), 6.4 (1H, s), 6.8 (2H, d, $J=8$), 7.0 (1H, t, $J=8$), 7.3 (2H, t, $J=8$), 7.5 (1H, t, $J=6$), 8.6 (2H, m).

Applying a similar procedure to ethyl 2-(2-fluoropyrid-3-yl)acetate gave 5-(2-fluoropyrid-3-yl)-5-methyl-3-phenylamino-2-thioxo-4-oxazolidinone, mp 130-135 °C.

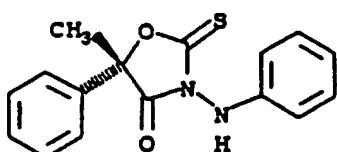
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EXAMPLE 7

10

(S)-5-Methyl-5-phenyl-3-phenylamino-2-thioxo-4-oxazolidinone

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20 A solution of 1.0 g (6.0 mmol) of (S)-atrolactic acid in 7 mL of methanol was cooled in an ice-water bath and stirred while 0.70 mL (1.15 g, 9.6 mmol) of thionyl chloride was added dropwise. The resulting mixture was stirred at room temperature for one hour, then concentrated under reduced pressure to give 1.1 g of methyl (S)-atrolactate, η_2^{25} 1.5096.

25 This material was dissolved in 10 mL of THF, and the solution was stirred and chilled in an ice-water bath while 0.68 g (6.1 mmol) of solid potassium tertiary-butoxide was added in one portion. The resulting slurry was stirred at room temperature for 40 minutes, then 0.40 mL (0.51 g, 6.7 mmol) of carbon disulfide was added, giving a solution. Ice-water cooling was resumed, and after 10 minutes 0.58 mL (0.66 g, 6.1 mmol) of ethyl chloroformate was added, giving a slurry.

30 After another 5 minutes 0.60 mL (0.66 g, 6.1 mmol) of phenyl hydrazine was added, cooling was removed, and the mixture was allowed to come to room temperature. Most of the THF was removed under reduced pressure, the residue was partitioned between water and 1-chlorobutane, and the organic phase was washed sequentially with 1N aqueous HCl, water, saturated aqueous sodium bicarbonate, and brine, dried over magnesium sulfate, and evaporated to leave 1.4 g of an oil. Chromatography over silica gel, eluting with methylene chloride-hexanes 70:30, provided 0.89 g (50%) of the title compound as an oil that slowly solidified on standing. Crystallization from 1-chlorobutane-hexanes 5:3 gave colorless needles: mp 81-85 °C; $[\alpha]_D^{23} +70.1$ ($c=0.52$, EtOH); IR (Nujol) 3250, 1775 cm⁻¹; NMR (CDCl₃, 200 MHz) 2.05 (3H, s), 6.37 (1H, s), 6.73 (2H, d, J=8), 7.02 (1H, t, J=8), 7.24 (2H, t, J=8), 7.4-7.5 (3H, m), 7.5-7.6 (2H, m).

35 Applying similar procedures to (R)-atrolactic acid gives (R)-3-(phenylamino)-5-phenyl-5-methyl-2-thioxo-4-oxazolidinone: mp 81-85 °C; $[\alpha]_D^{23} -70.5$ ($c=0.52$, EtOH).

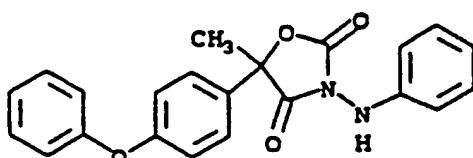
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EXAMPLE 8

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Preparation of 5-Methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione

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A solution of 5-methyl-5-(4-phenoxyphenyl)-3-phenylamino-2-thioxo-oxazolidin-4-one (2 g, 0.0051 moles) in 50 mls of acetone (0.1 M) was treated at room temperature with a solution of KHSO₅ (OXONE®, 4.72 g,

0.0154 moles) in 20 mls of water. The white slurry was heated at 50° C for two hours then cooled to room temperature and filtered. The residue was washed with fresh acetone and the filtrates were evaporated under reduced pressure until all the acetone distilled away. The residue was dissolved in methylene chloride and washed with water and brine. The organic layer was dried (MgSO_4), filtered, and evaporated to give the crude product. Recrystallization from 1-chlorobutane and petroleum ether afforded 1.68 g (88% of theoretical) of pure product as a white solid with a melting point of 140-142° C.

5 Tables I and II on the following pages show fungicidal compounds that can be advantageously prepared by the methods described above. These tables are illustrative of the invention only, and are not intended to be inclusive.

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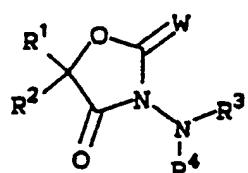
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TABLE 1

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	Ex#	W	R¹	R²	R³	R⁴	mp(°C)
25	1	S	Me	Ph	Ph	H	109 ¹
	2	S	Me	Ph	Ph	H	87 ²
	3	S	Me	Ph	Ph	H	87 ³
	4	S	H	Ph	Ph	H	142
30	5	S	Et	Ph	Ph	H	96
	6	S	n-hexyl	Ph	Ph	H	
	7	S	n-butyl	Ph	Ph	H	100
	8	S	CF ₃	Ph	Ph	H	
35	9	S	CF ₃ CH ₂ CH ₂ CH ₂	Ph	Ph	H	
	10	S	cyclopropyl	Ph	Ph	H	98
	11	S	cyclobutyl	Ph	Ph	H	oil
	12	S	cyclohexyl	Ph	Ph	H	
40	13	S	vinyl	Ph	Ph	H	107
	14	S	allyl	Ph	Ph	H	113
45							

¹racemic mixture²(R)-enantiomer³(S)-enantiomer

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55

	Ex#	N	R ¹	R ²	R ³	R ⁴	<u>mp(°C)</u>
5	15	S	acetylenyl	Ph	Ph	H	
	16	S	propargyl	Ph	Ph	H	
	17	S	methoxymethyl	Ph	Ph	H	
	18	S	cyclopropylmethyl	Ph	Ph	H	
10	19	S	benzyl	Ph	Ph	H	116
	20	S	4'-methoxybenzyl	Ph	Ph	H	
	21	S	4'-nitrobenzyl	Ph	Ph	H	
	22	S	4'-trifluoro- methylbenzyl	Ph	Ph	H	
15	23	S	4'-methylbenzyl	Ph	Ph	H	
	24	S	2',4'-dichloro- benzyl	Ph	Ph	H	
	25	S	4'-fluorobenzyl	Ph	Ph	H	
	26	S	Me	4-n-octylphenyl	Ph	H	
20	27	S	Me	4-(2-octenyl)phenyl	Ph	H	
	28	S	Me	4-(2-propenyl)phenyl	Ph	H	
	29	S	Me	4-(2-octenyl)phenyl	Ph	H	
	30	S	Me	4-n-octylthiophenyl	Ph	H	
25	31	S	Me	4-(1,1-dichloroallyl- phenyl	Ph	H	
	32	S	Me	4-(2-butynyl)phenyl	Ph	H	
	33	S	H	Me	Ph	H	117
	34	S	H	t-Bu	Ph	H	98
30	35	S	H	i-Pr	Ph	H	107
	40						
	45						
	50						

	EK1	W	R¹	R²	R³	R⁴	mp (°C)
5	36	S	H	cyclohexyl	Ph	H	90
	37	S	Me	Me	Ph	H	132
	38	S	benzyl	Me	Ph	H	99
10	39	S	Me	phenoxyethyl	Ph	H	77
	40	S	Me	n-hexyl	Ph	H	
15	41	S	Me	cyclohexyl	Ph	H	oil
	42	S	Me	4-chlorophenyl	Ph	H	156
	43	S	Me	3-chlorophenyl	Ph	H	105
20	44	S	Me	2-chlorophenyl	Ph	H	170
	45	S	Me	4-fluorophenyl	Ph	H	150
	46	S	Me	3-fluorophenyl	Ph	H	108
	47	S	Me	4-bromophenyl	Ph	H	115
25	48	S	Me	3,5-dichloro-phenyl	Ph	H	
	49	S	Me	3,4-dichloro-phenyl	Ph	H	143
	50	S	Me	2,4-dichloro-phenyl	Ph	H	161
30	51	S	Me	2-fluorophenyl	Ph	H	123
	52	S	Et	2-fluorophenyl	Ph	H	130
35	53	S	H	2-fluorophenyl	Ph	H	
	54	S	vinyl	2-fluorophenyl	Ph	H	102
	55	S	Me	2-fluorophenyl	4-fluoro-phenyl	H	129
40	56	S	Me	2-fluorophenyl	2-methyl-phenyl	H	129
	57	S	Me	2-fluorophenyl	4-methyl-phenyl	H	140
45	58	S	Me	2-fluorophenyl	2,6-di-chlorophenyl	H	148
	59						

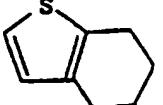
	Ex#	W	R¹	R²	R³	R⁴	mp(°C)
5	59	S	Me	2-fluorophenyl	Ph	Me	134
	60	S	Me	2,3-difluoro-phenyl	Ph	H	120
10	61	S	Me	2,5-difluoro-phenyl	Ph	H	119
	62	S	Me	3,5-difluoro-phenyl	Ph	H	135
15	63	S	Me	2,6-difluoro-phenyl	Ph	H	137
	64	S	Me	3,4-difluoro-phenyl	Ph	H	97
20	65	S	Me	2,4-difluoro-phenyl	Ph	H	127
	66	S	Et	2,4-difluoro-phenyl	Ph	H	
25	67	S	H	2,4-difluoro-phenyl	Ph	H	
	68	S	vinyl	2,4-difluoro-phenyl	Ph	H	
30	69	S	Me	2,4-difluoro-phenyl	Ph	Me	128
	70	S	Me	2,4-difluoro-phenyl	2,6-di-chlorophenyl	H	185
35	71	S	Me	2,4-difluoro-phenyl	4-fluoro-phenyl	H	136
	72	S	Me	2,4-difluoro-phenyl	4-methyl-phenyl	H	134
40	73	S	Me	2,4-difluoro-phenyl	2-methyl-phenyl	H	
	74	S	H	2-methylphenyl	Ph	H	121
45	75	S	Me	2-methylphenyl	Ph	H	115

	Expt	H	R¹	R²	R³	R⁴	mp(°C)
5	76	S	Me	4-methylphenyl	Ph	H	108
	77	S	Me	2,5-dimethyl-phenyl	Ph	H	
10	78	S	Me	4- <i>t</i> -butylphenyl	Ph	H	124
	79	S	Me	4-cyclohexyl-phenyl	Ph	H	160
15	80	S	Me	3-trifluoro-methylphenyl	Ph	H	133
	81	S	Me	3-nonafluorobutyl-phenyl	Ph	H	
20	82	S	Me	2-methoxyphenyl	Ph	H	
	83	S	Me	4-methoxyphenyl	Ph	H	156
	84	S	Me	4-ethoxyphenyl	Ph	H	64
25	85	S	Me	4- <i>n</i> -pentyloxy-phenyl	Ph	H	79
	86	S	Me	4-allyloxyphenyl	Ph	H	
30	87	S	Me	3-methylthio-phenyl	Ph	H	
	88	S	Me	4-trifluoro-methylthiophenyl	Ph	H	
35	89	S	Me	4-trifluoro-methoxyphenyl	Ph	H	
	90	S	Me	2-cyanophenyl	Ph	H	
40	91	S	Me	4-cyanophenyl	Ph	H	
	92	S	Me	2- <i>n</i> -pentyloxy-phenyl	Ph	H	146
45	93	S	Me	3- <i>n</i> -pentyloxy-phenyl	Ph	H	67
	94	S	Me	4-dimethylamino-phenyl	Ph	H	
50							

	Ex#	H	R¹	R²	R³	R⁴	<u>mp (°C)</u>
5	95	S	Me	4-(N-methyl-N-phenylamino)phenyl	Ph	H	
	96	S	Me	4-phenoxyphenyl	Ph	H	115
10	97	S	Et	4-phenoxyphenyl	Ph	H	
	98	S	H	4-phenoxyphenyl	Ph	H	
15	99	S	Me	4-phenoxyphenyl	Ph	Me	75
	100	S	Me	4-phenoxyphenyl	2-methyl-phenyl	H	139
20	101	S	Me	4-phenoxyphenyl	4-methyl-phenyl	H	
	102	S	Me	4'-phenoxyphenyl	4-fluoro-phenyl	H	
25	103	S	Me	3-phenoxyphenyl	Ph	H	oil
	104	S	Me	2-phenoxyphenyl	Ph	H	156
30	105	S	Me	4-(4-chloro-phenoxy)phenyl	Ph	H	114
	106	S	Me	4-(4-bromophenoxy-phenyl	Ph	H	111
35	107	S	Me	4-(4-fluoro-phenoxy)phenyl	Ph	H	137
	108	S	Me	4-(3-fluoro-phenoxy)phenyl	Ph	H	88
40	109	S	Me	4-(2-fluoro-phenoxy)phenyl	Ph	H	
	110	S	Me	4-(4-nitrophenoxy-phenyl	Ph	H	61
45	111	S	Me	4-(4-methyl-phenoxy)phenyl	Ph	H	
	112	S	Me	4-(2-methyl-phenoxy)phenyl	Ph	H	oil
50							

	Ex#	R	R¹	R²		R³	R⁴	mp(°C)
5	113	S	Me	4-benzylxyphenyl		Ph	H	157
	114	S	Me	2-fluoro-4- phenoxyphenyl		Ph	H	114
10	115	S	Me	4-carbomethoxy- phenyl		Ph	H	
	116	S	Me	4-carbophenoxy- phenyl		Ph	H	
15	117	S	Me	3-pyridyl		Ph	H	
	118	S	Me	4-pyridyl		Ph	H	
	119	S	Me	4-fluoro-3-pyridyl		Ph	H	
20	120	S	Me	3-fluoro-2-pyridyl		Ph	H	
	121	S	H	3-(3,5-dichloro- phenoxy)phenyl		Ph	H	130
25	122	S	H	3-(3-trifluoro- methylphenoxy)phenyl		Ph	H	oil
	123	S	H	3-phenoxyphenyl		Ph	H	136
30	124	S	Me	4-(4-trifluoro- methylphenoxy)phenyl		Ph	H	
	125	S	Me	4-(4-methoxy- phenoxy)phenyl		Ph	H	oil
35	126	S	Me	4-(2,4-dichloro- phenoxy)phenyl		Ph	H	121
	127	S	Me	4-methanesul- fonylphenyl		Ph	H	
40	128	S	Me	4-nitrophenyl		Ph	H	170
	129	S	Me	3-trifluoro- methylphenyl		Ph	H	134
45	130	S	Me	4-phenylthiophenyl		Ph	H	144
	131	S	Me	4-phenylphenyl		Ph	H	172
	132	S	Me	2-naphthyl		Ph	H	152
50								

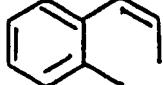
	Ex#	W	R ¹	R ²	R ³	R ⁴	<u>mp(°C)</u>
5	133	S	Me	1-naphthyl	Ph	H	139
	134	S	Me	2-thienyl	Ph	H	
	135	S	Me	5-chloro-2-thienyl	Ph	H	
	136	S	Me	4,5-dichloro-2-	Ph	H	132
10				thienyl			
	137	S	Me	5-methyl-2-thienyl	Ph	H	
	138	S	Me	3-methoxy-2-thienyl	Ph	H	
	139	S	Me	3-thienyl	Ph	H	121
15	140	S	Me	2,5-dichloro-3-thienyl	Ph	H	146
	141	S	Me	2,5-dimethyl-3-thienyl	Ph	H	88
	142	S	Me	2-phenoxy-3-thienyl	Ph	H	
	143	S	Me	2-nitro-4-thienyl	Ph	H	
20	144	S	Me	3-methoxy-4-thienyl	Ph	H	
	145	S	Me	2-furyl	Ph	H	
	146	S	Me	3-furyl	Ph	H	
	147	S	Me	2-pyridyl	Ph	H	
25	148	S	Me	5-fluoro-3-pyridyl	Ph	H	
	149	S	Me	2-fluoro-3-pyridyl	Ph	H	134
	150	S	Me	2-fluoro-4-pyridyl	Ph	H	
	151	S	Me	3-fluoro-4-pyridyl	Ph	H	168
30	152	S	-CH ₂ (CH ₂) ₃ CH ₂ -		Ph	H	oil
	153	S	-CH ₂ (CH ₂) ₃ CH ₂ -		3,5-dichloro-phenyl	H	184
35	154	S	-CH ₂ CH ₂ NMeCH ₂ CH ₂ -		Ph	H	
	155	S	-CH ₂ CH ₂ SCH ₂ CH ₂ -		Ph	H	
40							
45							
50							
55							

	Expt	R	R	R	R	<u>mp (°C)</u>
5	156 S			Ph	H	168
10	157 S			Ph	H	
15						
20	158 S			Ph	H	
25						
30	159 S Me		4-carbomethoxy- phenyl	Ph	H	
35	160 S Me		4-benzyl- phenyl	Ph	H	104
40	161 S			Ph	H	189
45	162 S Me		Ph	3,5-di- chlorophenyl	H	142
50	163 S cyclopropyl	Ph		3,5-di- chlorophenyl	H	133
55	164 S Me		phenoxy- methyl	3,5-di- chlorophenyl	H	146

	<u>Ex#</u>	<u>W</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp(°C)</u>
5	165	S Me	Ph		2,6-dichloro-phenyl	H	157
	166	S Me	4-phenoxy-phenyl		2,6-dichloro-phenyl	H	118
10	167	S Me	phenoxy-methyl		2,6-dichloro-phenyl	H	122
	168	S H	t-Bu		2,6-dichloro-phenyl	H	87
15	169	S Me	Ph		4-fluorophenyl	H	72
	170	S Me	4-fluorophenyl		4-fluorophenyl	H	91
20	171	S Me	4-cyclohexyl-phenyl		4-fluorophenyl	H	155
	172	S Me	phenylthiomethyl		4-fluorophenyl	H	68
25	173	S Me	Ph		3-fluorophenyl	H	70
	174	S Me	Ph		4-chlorophenyl	H	
30	175	S Me	Ph		3-chlorophenyl	H	132
	176	S Me	Ph		2-chlorophenyl	H	121
35	177	S Me	Ph		2-fluorophenyl	H	oil
	178	S Me	Ph		2,5-difluoro-phenyl	H	oil
40	179	S Me	Ph		2-bromophenyl	H	120
	180	S Me	Ph		4-methylphenyl	H	142
45	181	S Me	4-fluorophenyl		4-methylphenyl	H	106
	182	S Me	4-phenoxyphenyl		4-methylphenyl	H	146
50	183	S Me	phenylthiomethyl		4-methylphenyl	H	89
	184	S Me	phenoxymethyl		4-methylphenyl	H	155
55	185	S Me	2,5-dichloro-3-thienyl		4-methylphenyl	H	145

	Ex#	N R ¹ R ²	R ³	R ⁴	mp(°C)
5	186	S Me Ph	2,6-dimethylphenyl	H	101
	187	S Me Ph	4- <i>t</i> -butylphenyl	H	125
	188	S Me Ph	3-methylphenyl	H	97
10	189	S Me Ph	2-methylphenyl	H	100
	190	S Me Ph	2-methoxyphenyl	H	110
	191	S Me Ph	4-methoxyphenyl	H	135
15	192	S Me Ph	3-methoxyphenyl	H	oil
	193	S Me Ph	4- <i>n</i> -pentyloxyphenyl	H	oil
	194	S Me Ph	4-allyloxyphenyl	H	
20	195	S Me Ph	4-trifluoro- methoxyphenyl	H	73
	196	S Me Ph	4-trifluoromethyl- phenyl	H	
	197	S Me Ph	3-trifluoromethyl- phenyl	H	
25	198	S Me Ph	2-trifluoromethyl- phenyl	H	115
	199	S Me Ph	2-nitrophenyl	H	137
	200	S Me Ph	4-nitrophenyl	H	
30	201	S Me Ph	4-cyanophenyl	H	
	202	S Me Ph	4-carbomethoxy- phenyl	H	151
	203	S Me Ph	benzyl	H	82
35	204	S Me Ph	2-thienyl	H	
	205	S Me Ph	3-furyl	H	
	206	S Me Ph	2-pyridyl	H	147
40	207	S Me Ph	5-trifluoromethyl- 2-pyridyl	H	150

	<u>Expt No</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp(°C)</u>
5	208 S	Me	Ph	2-pyrimidyl	H	187
	209 S	Me	Ph	6-chloro- 3-pyridazyl	H	184
10	210 S	Me	Ph	ethyl	H	
	211 S	Me	Ph	cyclohexyl	H	
	212 S	Me	Ph	t-Bu	H	48
15	213 S	Me	Ph	n-hexyl	H	oil
	214 S	Me	Ph	n-decyl	H	
	215 S	Me	Ph	formyl		
	216 S	Me	Ph	acetyl		96
20	217 S	Me	Ph	trifluoro- acetyl		62
	218 S	Me	Ph	methoxy- acetyl		oil
25	219 S	Me	Ph	Ph	methoxy- carbonyl	
30	220 S	Me	Ph	Ph	methylamino- carbonyl	
	221 S	Me	Ph	Ph	methane- sulfonyl	
35	222 S	Me	3-thienyl	Ph	methyl	82
	223 S	4-fluoro- phenyl	Ph	Ph	methyl	118
40	224 S	Me	Ph	Ph	methyl	62
	225 S	Me	Ph	Ph	phenylamino- carbonyl	
45	226 S	Me	Ph	2-methyl- phenyl	methyl	oil
	227 S	Me	2,5-di- chloro-3- thienyl	Ph	methyl	147
50						

	Ex#	W	R¹	R²	R³	R⁴	mp(°C)
5	228	S	Me	4,5-dichloro- 2-thienyl	Ph	methyl	146
10	229	S	Me	Ph	Ph	ethyl	oil
15	230	S	Me	Ph	Ph	n-pentyl	
20	231	S	Me	3-thienyl	4-fluoro- phenyl	H	
25	232	S	Me	3-thienyl	4-fluoro- phenyl	acetyl	
30	233	S	Me	Ph	Ph	allyl	
35	234	S	Me	Ph	Ph	propargyl	
40	235	S	Me	Ph	Ph	cyclobutyl	
45	236	S	Me	Ph	Ph	benzyl	
50	237	S	Me	Ph			161
							
30	238	S	Me	Ph	Ph	2-bromo- propionyl	oil
35	239	S	Me	Ph	Ph	bromo- acetyl	112
40	240	S	Me	2,5-di- chloro-3- thienyl	Ph	methoxy- acetyl	82
45	241	S	Me	4,5-dichloro- 2-thienyl	Ph	methoxy- acetyl	80
50	242	S	Me	Ph	1-pyrrolo		80
	243	S	Me	4-fluoro- phenyl	1-pyrrolo		118
	244	S	Me	4-cyclohexyl- phenyl	1-pyrrolo		112

	Ex#	<u>R</u> ¹	<u>R</u> ²	<u>R</u> ³	<u>R</u> ⁴	<u>mp (°C)</u>
5	245	S Me	3-thienyl	1-pyrrolo		84
	246	O Me	Ph	Ph	H	163 ⁴
	247	O Me	Ph	Ph	H	92 ⁵
10	248	O H	Ph	Ph	H	
	249	O Et	Ph	Ph	H	
	250	O n-hexyl	Ph	Ph	H	
15	251	O CF ₃	Ph	Ph	H	
	252	O CF ₃ CH ₂ CH ₂ CH ₂	Ph	Ph	H	
	253	O cyclopropyl	Ph	Ph	H	
	254	O cyclohexyl	Ph	Ph	H	
20	255	O vinyl	Ph	Ph	H	
	256	O allyl	Ph	Ph	H	
	257	O acetylenyl	Ph	Ph	H	
25	258	O propargyl	Ph	Ph	H	
	259	O methoxymethyl	Ph	Ph	H	
	260	O cyclopropylmethyl	Ph	Ph	H	
	261	O benzyl	Ph	Ph	H	
30	262	O 4'-methoxybenzyl	Ph	Ph	H	
	263	O 4'-nitrobenzyl	Ph	Ph	H	
	264	O 4'-trifluoro-	Ph	Ph	H	
35		methylbenzyl				
	265	O 4'-methylbenzyl	Ph	Ph	H	
	266	O 2',4'-dichloro-	Ph	Ph	H	
40		benzyl				
	267	O Me	Ph	Ph	H	
	268	O Ph	4-n-octyl-	Ph	H	
			phenyl			

⁴racemic mixture⁵(S)-enantiomer

	<u>Ex#</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp(°C)</u>
5	269	O Me	4-n-octyl- thiophenyl	Ph	H	
10	270	O Me	4-(2-octenyl)- phenyl	Ph	H	
15	271	O Me	4-(2-octenoxy- phenyl	Ph	H	
20	272	O Me	4-(2-propenyl)- phenyl	Ph	H	
25	273	O Me	4-(2-butynyl)- phenyl	Ph	H	
30	274	O H	Me	Ph	H	
35	275	O H	i-Bu	Ph	H	
40	276	O H	i-Pr	Ph	H	
45	277	O H	cyclohexyl	Ph	H	
50	278	O Me	Me	Ph	H	115
55	279	O benzyl	Me	Ph	H	
	280	O Me	phenoxy-methyl	Ph	H	
	281	O Me	n-hexyl	Ph	H	
	282	O Me	4-chloro-phenyl	Ph	H	116
	283	O Me	3-chloro-phenyl	Ph	H	
	284	O Me	2-chloro-phenyl	Ph	H	
	285	O Me	4-fluoro-phenyl	Ph	H	102
	286	O Me	3-fluoro-phenyl	Ph	H	

	<u>Ex#</u>	<u>W</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp(°C)</u>
5	287	O	Me	4-bromo-phenyl	Ph	H	
	288	O	Me	3,5-dichloro-phenyl	Ph	H	
10	289	O	Me	3,4-dichloro-phenyl	Ph	H	
	290	O	Me	2,4-dichloro-phenyl	Ph	H	152
15	291	O	Me	2-fluorophenyl	Ph	H	149
	292	O	Et	2-fluorophenyl	Ph	H	
20	293	O	H	2-fluorophenyl	Ph	H	
	294	O	vinyl	2-fluorophenyl	Ph	H	
	295	O	Me	2-fluorophenyl	4-fluoro-phenyl		
25	296	O	Me	2-fluorophenyl	2-methyl-phenyl	H	140
	297	O	Me	2-fluorophenyl	4-methyl-phenyl	H	138
30	298	O	Me	2-fluorophenyl	2,6-dichlorophenyl	H	
	299	O	Me	2-fluorophenyl	Ph	Me	
	300	O	Me	2,3-difluoro-phenyl	Ph	H	
35	301	O	Me	2,5-difluoro-phenyl	Ph	H	141
	302	O	Me	3,5-difluoro-phenyl	Ph	H	
40	303	O	Me	2,6-difluoro-phenyl	Ph	H	
	304	O	Me	3,4-difluoro-phenyl	Ph	H	
45	305	O	Me	2,4-difluoro-phenyl	Ph	H	142
50							

	Ex#	H	R¹	R²	R³	R⁴	mp(°C)
5	306	O	Et	2,4-difluoro-phenyl	Ph	H	
	307	O	H	2,4-difluoro-phenyl	Ph	H	
10	308	O	vinyl	2,4-difluoro-phenyl	Ph	H	
	309	O	Me	2,4-difluoro-phenyl	Ph	Me	129
15	310	O	Me	2,4-difluoro-phenyl	2,6-dichlorophenyl	H	
	311	O	Me	2,4-difluoro-phenyl	4-fluoro-phenyl	H	
20	312	O	Me	2,4-difluoro-phenyl	4-methyl-phenyl	H	
	313	O	Me	2,4-difluoro-phenyl	2-methyl-phenyl	H	
25	314	O	Me	2-methylphenyl	Ph	H	140
	315	O	Me	4-methylphenyl	Ph	H	128
	316	O	Me	2,5-dimethyl-phenyl	Ph	H	
30	317	O	Me	4- <i>t</i> -butylphenyl	Ph	H	
	318	O	Me	4-cyclohexyl-phenyl	Ph	H	
35	319	O	Me	3-trifluoro-methylphenyl	Ph	H	
	320	O	Me	3-nonafluoro-butylphenyl	Ph	H	
40	321	O	Me	2-methoxyphenyl	Ph	H	
	322	O	Me	4-methoxyphenyl	Ph	H	104
45	323	O	Me	4- <i>n</i> -pentyloxy-phenyl	Ph	H	128
50							

	Ex#	W	R¹	R²	R³	R⁴	mp(°C)
5	324	O	Me	4-allyloxyphenyl	Ph	H	
	325	O	Me	3-methylthio-phenyl	Ph	H	
10	326	O	Me	4-trifluoro-methylthiophenyl	Ph	H	
	327	O	Me	4-trifluoro-methoxyphenyl	Ph	H	
15	328	O	M	2-cyanophenyl	Ph	H	
	329	O	Me	4-cyanophenyl	Ph	H	
	330	O	Me	4-phenoxyphenyl	Ph	H	142
20	331	O	Et	4-phenoxyphenyl	Ph	H	
	332	O	H	4-phenoxyphenyl	Ph	H	
	333	O	Me	4-phenoxyphenyl	Ph	Me	95
25	334	O	Me	4-phenoxyphenyl	2-methyl-phenyl	H	118
	335	O	Me	4-phenoxyphenyl	4-methyl-phenyl	H	
30	336	O	Me	4-phenoxyphenyl	4-fluoro-phenyl	H	
	337	O	Me	3-phenoxyphenyl	Ph	H	
35	338	O	Me	2-phenoxyphenyl	Ph	H	
	339	O	Me	4-(4-chlorophenoxy)-phenyl	Ph	H	
40	340	O	Me	4-(4-bromophenoxy)-phenyl	Ph	H	162
	341	O	Me	4-(4-fluorophenoxy)-phenyl	Ph	H	
45	342	O	Me	4-(3-fluorophenoxy)-phenyl	Ph	H	

	<u>Ex#</u>	<u>H</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp(°C)</u>
5	343	O	Me	4-(2-fluorophenoxy)-phenyl	Ph	H	
	344	O	Me	4-(4-nitrophenoxy)-phenyl	Ph	H	63
10	345	O	Me	4-(4-methylphenoxy)-phenyl	Ph	H	
	346	O	Me	4-(2-methylphenoxy)-phenyl	Ph	H	
15	347	O	Me	4-benzyloxyphenyl	Ph	H	
	348	O	Me	2-fluoro-4-phenoxyphenyl	Ph	H	129
20	349	O	Me	4-carbomethoxy-phenyl	Ph	H	
	350	O	Me	4-carbophenoxy-phenyl	Ph	H	
25	351	O	H	3-(3,5-dichlorophenoxy)phenyl	Ph	H	
	352	O	H	3-(3-trifluoromethylphenoxy)phenyl	Ph	H	
30	353	O	H	3-phenoxyphenyl	Ph	H	
	354	O	Me	4-(4-trifluoromethylphenoxy)phenyl	Ph	H	
35	355	O	Me	4-(4-methoxyphenoxy)phenyl	Ph	H	153
	356	O	Me	4-(2,4-dichlorophenoxy)phenyl	Ph	H	125
40	357	O	Me	4-methanesulfonylphenyl	Ph	H	
45							

	Ex#	W	R ¹	R ²	R ³	R ⁴	mp(°C)
5	358	O	Me	4-nitrophenyl	Ph	H	116
	359	O	Me	3-trifluoro- methylphenyl	Ph	H	
10	360	O	Me	4-phenylthiophenyl	Ph	H	
	361	O	Me	4-phenylphenyl	Ph	H	
	362	O	Me	2-naphthyl	Ph	H	
15	363	O	Me	1-naphthyl	Ph	H	
	364	O	Me	2-thienyl	Ph	H	
	365	O	Me	5-chloro-2-thienyl	Ph	H	
	366	O	Me	5-methyl-2-thienyl	Ph	H	
20	367	O	Me	3-methoxy-2-thienyl	Ph	H	
	368	O	Me	3-thienyl	Ph	H	146
	369	O	Me	2,5-dichloro-3-thienyl	Ph	H	
25	370	O	Me	2,5-dimethyl-3-thienyl	Ph	H	
	371	O	Me	2-phenoxy-3-thienyl	Ph	H	
	372	O	Me	2-nitro-4-thienyl	Ph	H	
30	373	O	Me	3-methoxy-4-thienyl	Ph	H	
	374	O	Me	2-furyl	Ph	H	
	375	O	Me	3-furyl	Ph	H	
35	376	O	Me	2-pyridyl	Ph	H	
	377	O	Me	3-pyridyl	Ph	H	
	378	O	Me	2-fluoro-3-pyridyl	Ph	H	
	379	O	Me	4-pyridyl	Ph	H	
40	380	O	Me	3-fluoro-4-pyridyl	Ph	H	131
	381	O	-CH ₂ (CH ₂) ₃ CH ₂ -		Ph	H	
	382	O	-CH ₂ (CH ₂) ₃ CH ₂ -		3,5- dichloro-		
45					phenyl		
	383	O	-CH ₂ CH ₂ NMeCH ₂ CH ₂ -		Ph	H	
50	384	O	-CH ₂ CH ₂ SCH ₂ CH ₂ -		Ph	H	

	Ex#	H	R ¹	R ²	R ³	R ⁴	mp(°C)
5	385	O			Ph	H	
10	386	O			Ph	H	
15	387	O Me		4-fluoro-3-pyridyl	Ph	H	
	388	O Me		3-fluoro-2-pyridyl	Ph	H	
20							
25	389	O			Ph	H	
30	390	O Me		4-carbomethoxy-phenyl	Ph	H	
35	391	O Me		4-benzyl-phenyl	Ph	H	
40	392	O			Ph	H	
45	393	O Me		Ph	3,5-di-chlorophenyl	H	
50	394	O cyclopropyl	Ph		3,5-di-chlorophenyl	H	

	Ex#	H	R¹	R²	R³	R⁴	mp(°C)
5	395	O Me	phenoxy-		3,5-di-	H	
			methyl		chlorophenyl		
10	396	O Me	Ph		2,6-dichloro-	H	
					phenyl		
15	397	O Me	4-phenoxy-		2,6-dichloro-	H	
			phenyl		phenyl		
20	398	O Me	phenoxy-		2,6-dichloro-	H	
			methyl		phenyl		
25	399	O H	t-Bu		2,6-dichloro-	H	
					phenyl		
30	400	O Me	Ph'		4-fluorophenyl	H	
	401	O Me	4-fluorophenyl		4-fluorophenyl	H	
	402	O Me	4-cyclohexyl-		4-fluorophenyl	H	
35	403	O Me	phenylthiomethyl		4-fluorophenyl	H	
	404	O Me	Ph		3-fluorophenyl	H	164
	405	O Me	Ph		4-chlorophenyl	H	
40	406	O Me	Ph		3-chlorophenyl	H	59
	407	O Me	4-methoxyphenyl		3-chlorophenyl	H	152
	408	O Me	Ph		2-fluorophenyl	H	
45	409	O Me	Ph		2,5-difluorophenyl	H	
	410	O Me	Ph		4-methylphenyl	H	
	411	O Me	4-fluorophenyl		4-methylphenyl		
50	412	O Me	4-phenoxyphenyl		4-methylphenyl		
	413	O Me	phenylthiomethyl		4-methylphenyl	H	
	414	O Me	phenoxyethyl		4-methylphenyl	H	
55	415	O Me	Ph		2,6-dimethylphenyl	H	
	416	O Me	Ph		4-t-butylphenyl	H	
	417	O Me	Ph		3-methylphenyl	H	
	418	O Me	Ph		2-methylphenyl	H	

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	Ex#	W	R ¹	R ²	R ³	R ⁴	mp(°C)
5	419	O	Me	Ph	4-methoxyphenyl	H	
	420	O	Me	Ph	4-n-pentyloxyphenyl	H	134
	421	O	Me	Ph	4-allyloxyphenyl	H	
10	422	O	Me	Ph	4-trifluoromethylphenyl	H	
	423	O	Me	Ph	3-trifluoromethylphenyl	H	
	424	O	Me	Ph	2-trifluoromethylphenyl	H	141
	425	O	Me	Ph	4-nitrophenyl	H	
15	426	O	Me	Ph	4-cyanophenyl	H	
	427	O	Me	Ph	4-carbomethoxyphenyl	H	
	428	O	Me	Ph	benzyl	H	
20	429	O	Me	Ph	2-thienyl	H	
	430	O	Me	Ph	3-furyl	H	
	431	O	Me	Ph	2-pyridyl	H	
25	432	O	Me	Ph	5-trifluoromethyl-2-pyridyl	H	
	433	O	Me	Ph	2-pyrimidyl	H	
30	434	O	Me	Ph	6-chloro-3-pyridazyl	H	
	435	O	Me	Ph	ethyl	H	
	436	O	Me	Ph	cyclohexyl	H	
	437	O	Me	Ph	5-Bu	H	
35	438	O	Me	Ph	n-decyl	H	
	439	O	Me	Ph	Ph	formyl	
	440	O	Me	Ph	Ph	acetyl	
40	441	O	Me	Ph	Ph	trifluoroacetyl	
	442	O	Me	Ph	Ph	methoxyacetyl	
	443	O	Me	Ph	Ph	methoxycarbonyl	
45	444	O	Me	Ph	Ph	methylaminocarbonyl	

	<u>Ex#</u>	<u>H</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp (°C)</u>
5	445	O Me		Ph	Ph	methane-sulfonyl	
	446	O Me	3-thienyl	Ph	Ph	methyl	118
10	447	O 4-fluoro-phenyl	Ph	Ph	Ph	methyl	
	448	O Me	Ph	Ph	Ph	methyl	131
15	449	O Me	Ph	Ph	Ph	phenylamino-carbonyl	
	450	O Me	Ph	Ph	Ph	allyl	
	451	O Me	Ph	Ph	Ph	propargyl	
20	452	O Me	Ph	Ph	Ph	cyclobutyl	
	453	O me	Ph	Ph	Ph	benzyl	
25	454	O Me	Ph				
30	455	O Me	2-cyano-phenyl	2-methyl-phenyl	H		
	456	O Me	2-N,N-dimethylamino-phenyl	Ph	H		
35							
	457	O Me	3-pyridyl	Ph	H		
40	458	O Me	4-pyridyl	Ph	H		
	459	S vinyl	phenyl	4-fluoro-phenyl	H		64
45	460	S Me	4-(6,6,6-trichlorohexyl-thio)phenyl	Ph	H		
50							

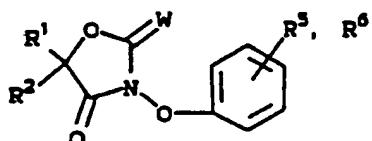
	Exi	H R¹	R²	R³	R⁴	mp(°C)
5	461	S Me	4-(6,6,6-tri- fluorohexyloxy- phenyl	Ph	H	
10	462	S Me	4-(trifluoro- methanesulfonyl)- phenyl	Ph	H	
15	463	S Me	4-(2'-fluoro- benzyloxy)- phenyl	Ph	H	
20	464	S Me	4-(4'-phenoxy- benzyloxy)- phenyl	Ph	H	
25	465	S Me	3-fluoro-4- phenoxyphenyl	Ph	H	
30	466	O Me	3-fluoro-4- phenoxyphenyl	Ph	H	
35	467	S Me	2-fluoro-4-(2- fluorophenoxy)- phenyl	Ph	H	
40	468	O Me	2-fluoro-4-(2- fluorophenoxy)- phenyl	Ph	H	
45	469	S Me	4-(2,4-di- fluoro- phenoxy)phenyl	Ph	H	
50	470	O Me	4-(2,4-di- fluoro- phenoxy)phenyl	Ph	H	
55	471	S Me	4-(4-n-butyloxy- phenoxy)phenyl	Ph	H	
	472	S Me	4-(4-n-butyl- phenoxy)phenyl	Ph	H	

	Ex#	H R¹	R²	R³	R⁴	mp(°C)
5	473	S Me	4-(4-cyclo- hexyloxy- phenoxy)phenyl	Ph	H	
10	474	S Me	4-(4-methoxy- methyl)phenyl	Ph	H	
15	475	S Me	4-phenethyloxy- phenyl	Ph	H	
20	476	S Me	4-(2'-fluoro- phenyl	Ph	H	
25	477	S Me	Ph	4-fluoro- 2-methyl- phenyl	H	
30	478	S Me	4-(N-phenyl- amino)phenyl	Ph	H	
35	479	S Me	4-(N-methyl- amino)phenyl	Ph	H	
40	480	O Me	4-(N-methyl- amino)phenyl	Ph	H	
45	481	S Me	4-(N-butyl- amino)phenyl	Ph	H	
50	482	S Me	4-(N-(2-fluoro- phenyl)amino)- phenyl	Ph	H	
55	483	S Me	4-(N-(4-methyl- phenyl)amino)- phenyl	Ph	H	

TABLE 2

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	<u>Expt</u>	<u>W</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>R⁴</u>	<u>mp (°C)</u>
20							
	484	S	Me	Ph	H	H	
	485	O	Me	Ph	H	H	
25	486	S	H	Ph	H	H	
	487	S	trifluoro- methyl	Ph	H	H	
30	488	S	Me	3-thienyl	H	H	
	489	S	Me	4-fluorophenyl	H	H	
	490	S	Me	2,4-difluoro- phenyl	H	H	82
35	491	S	Me	4-phenoxyphenyl	H	H	oil
	492	S	Me	3-trifluoro- methylphenyl	H	H	
40	493	S	Me	Ph	4-fluoro	H	
	494	S	Me	Ph	3-trifluoro- methyl	H	
45	495	S	Me	Ph	4-phenoxy	H	
	496	S	Me	Ph	2-chloro	4-chloro	
	497	S	Me	Ph	2-Me	6-Me	

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Formulation

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The compounds of this invention will generally be used in formulation with a liquid or solid diluent or with an organic solvent. Useful formulations of the compounds of Formula I can be prepared in conventional ways. They include dusts, granules, pellets, solutions, emulsions, wettable powders, emulsifiable con-

centrates and the like. Many of these may be applied directly. Sprayable formulations can be extended in suitable media and used at spray volumes of from about one to several hundred liters per hectare. High strength compositions are primarily used as intermediates for further formulation. The formulations, broadly, contain about 1% to 99% by weight of active ingredient(s) and at least one of a) about 0.1% to 35% surfactant(s) and b) about 5% to 99% solid or liquid inert diluent(s). More specifically, they will contain these ingredients in the following approximate proportions:

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	Percent by Weight		
	Active Ingredient	Diluent(s)	Surfactant(s)
Wettable Powders	20-90	0-74	1-10
Oil Suspensions, Emulsions, Solutions, (including Emulsifiable Concentrates)	5-50	40-95	0-35
Aqueous Suspensions	10-50	40-84	1-20
Dusts	1-25	70-99	0-5
Granules and Pellets	1-95	5-99	0-15
High Strength Compositions	90-99	0-10	0-2

Lower or higher levels of active ingredient can of course, be present depending on the intended use and the physical properties of the compound. Higher ratios of surfactant to active ingredient are sometimes desirable, and are achieved by incorporation into the formulation or by tank mixing.

- 5 Typical solid diluents are described in Watkins, et al., "Handbook of Insecticide Dust Diluents and Carriers", 2nd Ed., Dorland Books, Caldwell, New Jersey. The more absorptive diluents are preferred for the wettable powders and the denser ones for dusts. Typical liquid diluents and solvents are described in Marsden, "Solvents Guide," 2nd Ed., Interscience, New York, 1950. Solubility under 0.1% is preferred for suspension concentrates; solution concentrates are preferably stable against phase separation at 0°C.
- 10 "McCutcheon's Detergents and Emulsifiers Annual", MC Publishing Corp., Ridgewood, New Jersey, as well as Sisely and Wood, "Encyclopedia of Surface Active Agents", Chemical Publ. Co., Inc., New York, 1964, list surfactants and recommended uses. All formulations can contain minor amounts of additives to reduce foam, caking, corrosion, microbiological growth, etc. Preferably, ingredients should be approved by the U.S. Environmental Protection Agency for the use intended.
- 15 The methods of making such compositions are well known. Solutions are prepared by simply mixing the ingredients. Fine solid compositions are made by blending and, usually, grinding as in a hammer or fluid energy mill. Suspensions are prepared by wet milling (see, for example, Littler, U.S. Patent 3,060,084). Granules and pellets may be made by spraying the active material upon preformed granular carriers or by agglomeration techniques. See J. E. Browning, "Agglomeration", Chemical Engineering, Dec. 4, 1967, pp. 147ff. and "Perry's Chemical Engineer's Handbook", 4th Edn., McGraw-Hill, N.Y., 1963, pp. 8-59ff.
- 20 For further information regarding the art of formulation, see for example:
H. M. Loux, U.S. Patent 3,235,361, Feb. 15, 1966, Col. 6, Line 16 through Col. 7, Line 19 and Examples 10 through 41.
R. W. Luckenbaugh, U.S. Patent 3,309,192, March 14, 1967, Col. 5, Line 43 through Col. 7, Line 62 and Examples 8, 12, 15, 39, 41, 52, 53, 58, 132, 138-140, 162-164, 166, 167, 169-182.
- 25 H. Gysin and E. Knusli, U.S. Patent 2,891,855, June 23, 1959, Col. 3, Line 66 through Col. 5, Line 17 and Examples 1-4.
G. C. Klingman, "Weed Control as a Science", John Wiley and Sons, Inc., New York, 1961, pp. 81-96.
J. D. Fryer and S. A. Evans, "Weed Control Handbook", 5th Edn. Blackwell Scientific Publications, Oxford,
- 30 1968, pp. 101-103.
Examples of useful formulations of compounds of the present invention are as follows.

EXAMPLES

35

EXAMPLE 217

40

Wettable Powder	
	5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone
	Sodium Alkylnaphthalenesulfonate
	Sodium Ligninsulfonate
	Synthetic Amorphous Silica
	Kaolinite
	80%
	4%
	2%
	1%
	13%

45

The ingredients are blended, hammermilled, re-blended and packaged.

EXAMPLE 218

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High Strength Concentrate		
5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone	98.5%	
Silica Aerogel	0.5%	
Synthetic Amorphous Silica	1.0%	

10 The ingredients are blended and ground in a hammermill to produce a high strength concentrate essentially all passing a U.S.S. No. 50 Sieve (0.3 mm openings). This material may then be formulated in a variety of ways.

EXAMPLE 219

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Solution		
5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone	25%	
N-methyl-2-pyrrolidone	75%	

25 The ingredients are combined and stirred to produce a solution, which can be used for low volume applications.

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EXAMPLE 220

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Emulsifiable Concentrate		
5-methyl-5-phenyl-3-(phenylamino)-2-thioxo-4-oxazolidinone	15%	
Blend of calcium sulfonates and non-ionic surfactants	6%	
Acetophenone	79%	

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The ingredients are combined and stirred until the active is dissolved. A fine screen filter is included in packaging operation to insure the absence of any extraneous undissolved material in the product.

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Utility

45 The compounds of this invention are useful as plant disease control agents. They provide control of diseases caused by a broad spectrum of plant pathogens in the basidiomycete, and ascomycete classes and particularly against fungi in the oomycete class. They are effective in controlling a broad spectrum of plant diseases, particularly foliar pathogens of ornamental, vegetable, field, cereal and fruit crops, such as Plasmopara viticola, Phytophthora infestans, Peronospora tabacina, Pseudoperonospora cubensis, Phytophthora megasperma, Botrytis cinerea, Venturia inaequalis, Puccinia recondita, Pythium aphanidermatum, Alternaria brassicola, Septoria nodorum, Cercosporidium personatum and species related to these pathogens.

50 The compounds of this invention can be mixed with fungicides, bactericides, acaricides, nematicides, insecticides or other biologically active compounds in order to achieve desired results with a minimum of expenditure of time, effort and material. Suitable agents of this type are well-known to those skilled in the art. Some are listed below:

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Fungicides

methyl 2-benzimidazolecarbamate (carbendazim)
tetramethylthiuram disulfide (thiuram)
n-dodecylguanidine acetate (dodine)

- manganese ethylenebisdithiocarbamate (maneb)
 1,4-dichloro-2,5-dimethoxybenzene (chloroneb)
 methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate (benomyl)
 2-cyano-N-ethylcarbamoyl-2-methoxyiminoacetamide (cymoxanil)
- 5 N-trichloromethylthiotetrahydrophthalimide (captan)
 N-trichloromethylthiophthalimide (folpet)
 dimethyl 4,4'-(*o*-phenylene)bis(3-thioallophanate) (thiophanate-methyl)
 2-(thiazol-4-yl)benzimidazole (thiabendazole)
 aluminum tri(O-ethyl phosphonate)(phosethyl aluminum)
- 10 tetrachloroisophthalonitrile (chlorothalonil)
 2,6-dichloro-4-nitroaniline (dichloran)
 N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine methyl ester (metalaxyl)
 cis-N-[1,1,2,2-tetrachloroethyl]thiocyclohex-4-ene-1,2-dicarboximide (captafol)
 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine carboxamide (iprodione)
- 15 3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione (vinclozolin)
 kasugamycin
 O-Ethyl-S,S-diphenylphosphorodithioate (edifenphos)
 4-(3-(4-(1,1-dimethylethyl)phenyl)-2-methyl)propyl-2,6-dimethylmorpholine (fenpropimorph)
 4-(3-(4-(1,1-dimethylethyl)phenyl)-2-methyl)propylpiperidine (fenpropidine)
- 20 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butane (triadimefon)
 2-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)hexanenitrile (myclobutanil)
 tebuconazol
 3-chloro-4-[4-methyl-2-(1H-1,2,4-triazol)-1-ylmethyl]-1,3-dioxolan-2-yl]phenyl-4-chlorophenylether (difenaconazole)
- 25 1-[2-(2,4-dichlorophenyl)pentyl]1H-1,2,4-triazole (penconazole)
 α -(2-fluorophenyl)- α -(4-fluorophenyl)-1H-1,2,4-triazole-1-ethanol (flutriafol)
 2-methoxy-N-(2-oxo-1,3-oxazolidin-3-yl)acet-2,6-xylidide (oxadixyl)
 1-[[bis(4-fluorophenyl)methylsilyl]methyl]-1H-1,2,4-triazole (flusilazole)
 1-N-propyl-N-[2(2,4,6-trichlorophenoxy)ethyl]carbamoylimidazole (prochloraz)
- 30 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole (propiconazole)
 α -(2-chlorophenyl)- α -(4-chlorophenyl)-5-pyridinemethanol (fenarimol)
 copper oxychloride
 methyl N-(2,6-dimethyl-phenyl)-N-(2-furanylcarbonyl)-DL-alaninate (furalaxyd)
 hexaconazole
- 35 4-chloro-N-(cyanoethoxymethyl)benzamide
 4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-1-oxo-2-propenyl]morpholine
- Bactericides
 tribasic copper sulfate
 streptomycin sulfate
- 40 oxytetracycline
Acaricides
 senecioic acid, ester with 2-sec-butyl-4,6-dinitrophenol (binapacryl)
 6-methyl-1,3-dithiolo[2,3-B]quinonolin-2-one (oxythioquinox)
 2,2,2-trichloro-1,1-bis(4-chlorophenyl)ethanol (dicofol)
- 45 bis(pentachloro-2,4-cyclopentadien-1-yl) (dienochlor)
 tricyclohexyltin hydroxide (cyhexatin)
 hexakis(2-methyl-2-phenylpropyl)distannoxane (fenbutin oxide)
- Nematicides
 2-[diethoxyphosphinylimino]-1,3-diethietane (fosthietan)
- 50 S-methyl-1-(dimethylcarbamoyl)-N-(methylcarbamoyloxy)thioformimidate (oxamyl)
 S-methyl-1-carbamoyl-N-(methylcarbamoyloxy)thioformimidate
 N-isopropylphosphoramidic acid, O-ethyl-O'-[4-(methylthio)-*m*-tolyl]diester (fenamiphos)
- Insecticides
 3-hydroxy-N-methylcrotonamide(dimethylphosphate)ester (monocrotophos)
 55 methylcarbamic acid, ester with 2,3-dihydro-2,2-dimethyl-7-benzofuranol (carbofuran)
 O-[2,4,5-trichloro- α -(chloromethyl)benzyl]phosphoric acid, O,O'-dimethyl ester (tetrachlorvinphos)
 2-mercaptosuccinic acid, diethyl ester, S-ester with thionophosphoric acid, dimethyl ester (malathion)
 phosphorothioic acid, O,O-dimethyl, O-*p*-nitrophenyl ester (methyl parathion)

- methylcarbamic acid, ester with α -naphthol (carbaryl)
 methyl N-[(methylamino)carbonyl]oxyethanimidothioate (methomyl)
 N'-(4-chloro-o-tolyl)-N,N-dimethylformamidine (chlorodimeform)
 O,O-diethyl-O-(2-isopropyl-4-methyl-6-pyrimidyl)phosphorothioate (diazinon)
- 5 octachlorocamphene (toxaphene)
 O-ethyl O-p-nitrophenyl phenylphosphonothioate (EPN)
 cyano(3-phenoxyphenyl)-methyl 4-chloro- α -(methyl ethyl)benzeneacetate (fenvalerate)
 (3-phenoxyphenyl)methyl (\pm -)cis,trans-3-(2,2-dichloroethyl)-2,2-dimethylcyclopropanecarboxylate
 (permethrin)
- 10 dimethyl N,N'-[thiobis(N-methylimino)carbonyloxy]]bis[ethanimidothioate] (thiodicarb)
 phosphorothiolothionic acid, O-ethyl-O-[4-(methylthio)phenyl]-S-n-propyl ester (sulprofos)
 α -cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate (cypermethrin)
 cyano(3-phenoxyphenyl)methyl 4-(difluoromethoxy)- α -(methyl ethyl)benzeneacetate (flucythrinate)
 O,O-diethyl-O-(3,5,6-trichloro-2-pyridyl)phosphorothioate (chlorpyrifos)
- 15 15 O,O-dimethyl-S-[(4-oxo-1,2,3-benzotriazin-3-(4H)-yl)methyl]phosphorothioate (azinphos-methyl)
 5,6-dimethyl-2-dimethylamino-4-pyrimidinyl dimethyl carbamate (pirimicarb)
 S-(N-formyl-N-methylcarbamoylmethyl)-O,O-dimethyl phosphorothioate (formothion)
 S-2-(ethylthioethyl)-O,O-dimethyl phosphorothioate (demeton-S-methyl)
 α -cyano-3-phenoxybenzyl cis-3(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate (deltamethrin)
- 20 cyano(3-phenoxyphenyl)methyl ester of N-(2-chloro-4-trifluoromethylphenyl)alanine (fluvalinate)
- In some instances, combinations with other fungicides having a similar spectrum of disease control but a different mode of action will be particularly advantageous for resistance management and/or improved properties such as curative activity for established infections. A particularly effective combination in both regards is one involving a compound of Formula I and cynoxanil.

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Application

- Disease control is ordinarily accomplished by applying an effective amount of the compound either pre-
 30 or post-infection to the portion of the plant to be protected such as the roots, stems, foliage, fruit, seeds, tubers or bulbs. The compound may also be applied to the seed from which the plants to be protected are to be grown.

- Rates of application for these compounds can be influenced by many factors of the environment and should be determined under actual use conditions. Foliage can normally be protected when treated at a rate
 35 of from less than 1 g/ha to 10,000 g/ha of active ingredient. Seed and seedlings can normally be protected when seed is treated at a rate of from .1 to 10 grams per kilogram of seed.

EXAMPLE A

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- The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). This suspension was sprayed to the point of run-off on apple seedlings. The
 45 following day the seedlings were inoculated with a spore suspension of Venturia inaequalis (the causal agent of apple scab) and incubated in a saturated atmosphere at 20° C for 24 hr, and then moved to a growth chamber at 22° C for 11 days, after which disease ratings were made.

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EXAMPLE B

- The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). This suspension was sprayed to the point of run-off on peanut seedlings. The
 55 following day the seedlings were inoculated with a spore suspension of Cercosporidium personatum (the causal agent of peanut late leafspot) and incubated in a saturated atmosphere at 22° C for 24 hr, a high humidity atmosphere at 22 to 30° C for 5 days, and then moved to a growth chamber at 29° C for 6 days.

after which disease ratings were made.

EXAMPLE C

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The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). This suspension was sprayed to the point of run-off on wheat seedlings. The 10 following day the seedlings were inoculated with a spore suspension of Puccinia recondita (the causal agent of wheat leaf rust) and incubated in a saturated atmosphere at 20 °C for 24 hr, and then moved to a growth chamber at 20 °C for 6 days, after which disease ratings were made.

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EXAMPLE D

The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). This suspension was sprayed to the point of run-off on tomato seedlings. The 20 following day the seedlings were inoculated with a spore suspension of Phytophthora infestans (the causal agent of potato and tomato late blight) and incubated in a saturated atmosphere at 20 °C for 24 hr, and then moved to a growth chamber at 20 °C for 5 days, after which disease ratings were made.

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EXAMPLE E

The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 40 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). The suspension was sprayed to the point of run-off on grape seedlings. The 30 following day the seedlings were inoculated with a spore suspension of Plasmopara viticola (the causal agent of grape downy mildew) and incubated in a saturated atmosphere at 20 °C for 24 hours, moved to a growth chamber at 20 °C for 6 days, and then incubated in a saturated atmosphere at 20 °C for 24 hours, 35 after which the disease ratings were made.

EXAMPLE F

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The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). This suspension was sprayed to the point of run-off on cucumber seedlings. The 45 following day the seedlings were inoculated with a spore suspension of Botrytis cinerea (the causal agent of gray mold on many crops) and incubated in a saturated atmosphere at 20 °C for 48 hr, and moved to a growth chamber at 20 °C for 5 days, after which disease ratings were made.

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EXAMPLE G

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The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then suspended at a concentration of 40 ppm in purified water containing 250 ppm of the surfactant Trem 014 (polyhydric alcohol esters). The suspension was sprayed to the point of run-off on tobacco seedlings. The following day the seedlings were inoculated with a spore suspension of Peronospora tabacina (the causal agent of tobacco blue mold) and incubated in a saturated atmosphere at 20 °C for 24 hours, moved to a growth chamber at 22 °C for 6 days, and then incubated in a saturated atmosphere at 20 °C for 24 hours, after which the disease ratings were made.

EXAMPLE H

The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then
5 suspended at a concentration of 40 ppm in purified water containing 250 ppm of the surfactant Trem 014
(polyhydric alcohol esters). The suspension was sprayed to the point of run-off on cucumber seedlings. The
following day the seedlings were inoculated with a spore suspension of Pseudoperonospora cubensis (the
causal agent of cucumber downy mildew) and incubated in a saturated atmosphere at 20 °C for 24 hours,
moved to a growth chamber at 20 °C for 6 days, and the incubated in a saturated atmosphere at 20 °C for
10 24 hours, after which the disease ratings were made.

EXAMPLE I

15 The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then
suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014
(polyhydric alcohol esters). The suspension was sprayed to the point of run-off on wheat seedlings. The
following day the seedlings were inoculated with spores of Erysiphe graminis (the causal agent of wheat
20 powdery mildew) and incubated in a growth chamber at 20 °C for 7 days after which disease ratings were
made.

EXAMPLE J

25 The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then
suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014
(polyhydric alcohol esters). The suspension was sprayed to the point of run-off on rice seedlings.
30 The following day the seedlings were inoculated with a spore suspension of Rhizoctonia solani (the
causal agent of rice sheath blight) and incubated in a saturated atmosphere at 27 °C for 48 hours, moved to
a growth chamber at 29 °C for 48 hours after which the disease ratings were made.

EXAMPLE K

The test compounds were dissolved in acetone in an amount equal to 3% of the final volume and then
40 suspended at a concentration of 200 ppm in purified water containing 250 ppm of the surfactant Trem 014
(polyhydric alcohol esters). The suspension was sprayed to the point of run-off on rice seedlings. The
following day the seedlings were inoculated with a spore suspension of Pyricularia oryzae (the causal agent
of rice blast) and incubated in a saturated atmosphere at 27 °C for 24 hours, moved to a growth chamber at
30 °C for 4 days after which the disease ratings were made.
Examples which further illustrate the invention can be found in the following table. In the table, a rating
45 of 100 indicates 100% disease control and a rating of 0 indicates no disease control (relative to the carrier
sprayed controls). A "-" indicates that no test was performed at the indicated concentration on that disease.

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CMPD NO.	EX. A	EX. B	EX. C	EX. D	EX. E	EX. F	EX. G	EX. H	EX. I	EX. J	EX. K
5	278	36	0	-	0	-	45	-	-	0	0
	169	64	71	-	64	100	0	70	46	0	0
	156	39	43	-	77	100	96	-	-	0	0
10	212	50	0	-	0	22	0	-	-	0	0
	3	97	100	100	99	100	0	100	100	0	73
	2	92	60	-	0	54	5	0	11	0	0
15	76	0	0	-	92	100	0	-	-	0	0
	75	69	18	-	21	99	7	-	-	0	0
	208	81	34	-	76	72	0	-	-	0	0
20	207	4	34	-	0	35	0	-	-	0	0
	206	51	33	-	25	68	0	-	-	0	0
	13	93	64	-	93	54	0	-	-	0	0
	131	30	11	-	0	14	0	-	-	0	0
25	186	60	60	-	0	65	0	-	-	63	0
	193	23	64	-	0	29	0	-	-	0	0
	161	60	26	-	0	86	69	-	-	39	0
30	42	61	79	-	93	97	0	92	79	60	0
	282	39	23	-	0	88	0	62	67	0	0
	45	88	23	-	99	100	0	100	100	34	0
35	285	11	23	-	93	99	0	99	100	60	0
	83	61	58	-	64	100	0	55	62	0	0
	322	11	23	-	86	75	0	0	-	34	0
40	128	61	23	-	64	25	0	0	-	34	0
	358	39	23	-	0	32	0	0	-	0	0
	1	59	91	100	99	100	-	100	-	0	0
45	37	77	23	-	0	17	0	0	-	34	0

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CMPD NO.	EX. A	EX. B	EX. C	EX. D	EX. E	EX. F	EX. G	EX. H	EX. I	EX. J	EX. K	
5	175	39	23	-	86	97	0	36	-	0	0	0
	406	61	23	-	0	-	0	46	-	34	0	0
	38	39	0	-	0	49	0	0	-	0	0	0
10	96	61	23	-	26	100	0	100	100	0	0	22
	407	61	0	-	0	34	0	0	-	0	0	22
	246	39	23	-	47	98	0	91	100	0	0	0
15	139	0	43	-	99	100	88	92	89	0	0	0
	152	6	0	-	47	48	35	0	0	39	0	0
	153	0	0	-	0	15	0	0	0	0	0	0
20	35	0	0	-	0	23	96	0	0	0	0	0
	34	64	0	-	0	-	88	0	11	39	0	0
	4	39	0	-	47	97	99	0	25	0	0	0
25	36	81	0	-	26	15	79	0	6	0	0	0
	216	39	94	-	26	45	35	13	11	39	0	0
	19	39	0	-	0	79	63	0	39	0	0	0
	224	6	43	-	77	82	0	32	46	39	0	27
30	162	39	43	-	0	89	0	0	11	0	0	0
	5	81	0	-	0	-	0	0	0	0	0	0
	10	6	43	-	0	77	0	0	0	0	0	0
35	163	39	0	-	0	58	35	0	6	0	0	0
	171	-	-	-	-	36	-	0	4	-	-	-
	14	-	-	-	-	34	-	0	22	-	-	-
40	39	-	-	-	-	53	-	0	11	-	-	-
	191	11	23	-	0	73	0	0	-	0	0	0
	322	61	23	-	0	0	0	0	-	0	0	0
45	218	-	-	-	-	100	-	66	11	-	-	-
	79	-	-	-	-	13	-	0	58	-	-	-
	184	-	-	-	-	13	-	4	4	-	-	-
	164	-	-	-	-	62	-	0	7	-	-	-
50	167	-	-	-	-	3	-	9	4	-	-	-
	172	-	-	-	-	58	-	0	38	-	-	-

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CMPD NO.	EX. A	EX. B	EX. C	EX. D	EX. E	EX. F	EX. G	EX. H	EX. I	EX. J	EX. K
5	183	-	-	-	58	-	0	7	-	-	-
	33	-	-	-	4	-	0	7	-	-	-
10	169	-	-	-	100	-	47	36	-	-	-
	168	-	-	-	59	-	0	29	-	-	-
	180	-	-	-	100	-	0	49	-	-	-
15	165	-	-	-	15	-	0	11	-	-	-
	181	-	-	-	100	-	77	22	-	-	-
	170	-	-	-	100	-	17	49	-	-	-
	182	-	-	-	15	-	21	22	-	-	-
20	166	-	-	-	2	-	0	40	-	-	-
	54	46	21	-	86	89	0	-	-	0	0
	65	46	98	-	100	100	0	100	100	0	0
25	70	0	21	-	0	0	0	-	-	0	0
	80	0	11	-	0	3	6	-	-	0	0
	209	0	0	-	0	12	6	-	-	0	0
30	132	30	11	-	0	43	90	-	-	0	0
	78	0	11	-	0	25	6	-	-	0	0
	49	0	0	-	0	100	0	-	-	0	0
	177	97	39	98	25	95	99	-	-	37	0
35	178	91	0	-	25	74	0	-	-	0	0
	47	100	39	-	76	97	0	-	-	0	0
	188	92	76	-	47	91	0	-	-	54	0
40	237	100	0	-	0	8	0	-	-	0	0
	123	100	0	-	24	0	0	-	-	0	0
	121	-	-	-	-	39	-	-	-	-	-
45	174	0	46	-	0	-	0	-	-	0	0
	189	80	72	-	99	100	0	-	-	0	0
	459	46	0	-	0	36	8	-	-	0	0
	46	30	100	99	99	100	0	42	23	0	19
50	11	0	0	-	0	22	0	-	-	0	0
	7	0	57	-	0	62	0	-	-	0	0

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CMPD NO.	EX. <u>A</u>	EX. <u>B</u>	EX. <u>C</u>	EX. <u>D</u>	EX. <u>E</u>	EX. <u>F</u>	EX. <u>G</u>	EX. <u>H</u>	EX. <u>I</u>	EX. <u>J</u>	EX. <u>K</u>	
5	133	51	0	-	0	45	0	-	-	0	0	0
	130	51	40	-	0	97	0	-	-	0	0	0
10	122	25	0	-	0	44	0	-	-	0	0	0
	44	68	21	-	0	98	47	-	-	0	0	0
	84	85	0	-	99	98	5	-	-	38	0	0
15	85	71	82	-	0	100	0	-	-	0	36	27
	106	93	35	-	24	100	5	-	-	38	0	0
	113	0	0	-	46	100	5	-	-	0	0	0
	62	0	65	-	46	100	5	-	-	0	0	0
20	78	51	0	-	0	88	5	-	-	0	0	0
	160	0	82	-	46	100	0	-	-	0	0	85
	192	91	78	-	97	97	6	-	-	0	0	0
25	176	61	22	-	0	99	0	-	-	38	0	0
	60	61	100	-	99	100	0	69	100	0	62	97
	199	0	79	0	0	-	0	-	-	39	0	25
30	179	60	59	-	0	-	0	-	-	39	0	25
	43	35	95	-	93	100	6	-	-	0	0	27
	92	0	0	-	0	7	0	-	-	0	0	0
	93	0	24	-	26	40	0	-	-	0	0	0
35	103	32	90	-	26	99	0	-	-	0	0	0
	63	32	79	100	99	100	0	-	-	0	0	0
	61	79	90	100	99	100	42	-	-	0	0	25
40	74	39	12	-	26	27	0	-	-	23	0	0
	238	5	95	-	0	-	0	-	-	54	0	0
	330	11	83	100	93	100	45	100	100	0	0	27
45	190	11	0	-	0	-	5	-	-	0	0	0
	104	43	0	-	0	5	0	-	-	36	0	27
	202	11	0	-	26	94	5	-	-	0	0	0
	247	64	81	-	97	100	0	-	-	0	0	67
50	195	17	0	-	26	-	89	-	-	38	0	0
	198	15	26	-	0	-	66	-	-	0	0	0

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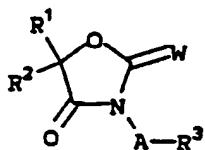
	CMPD NO.	EX. A	EX. B	EX. C	EX. D	EX. E	EX. F	EX. G	EX. H	EX. I	EX. J	EX. K
5	41	92	21	-	46	98	0	-	-	0	0	26
10	64	85	65	-	92	100	0	-	-	62	0	0
15	213	39	12	-	0	-	0	-	-	0	0	0
20	203	43	0	-	0	5	0	-	-	0	0	0
25	107	15	0	-	26	100	66	-	-	0	0	0
30	342	-	-	-	98	100	-	-	-	-	-	-
35	105	15	60	-	26	-	80	-	-	0	0	0
40	51	0	100	-	97	100	80	-	-	38	0	0
45	108	3	96	100	76	100	0	-	-	0	0	86
50	305	0	79	-	99	100	0	-	-	0	0	28
55	114	87	96	-	97	-	0	-	-	0	0	94
60	229	3	24	-	24	-	0	-	-	0	0	0
65	230	42	0	-	0	-	0	-	-	0	0	0
70	226	51	0	-	0	-	-	-	-	0	36	67
75	239	73	60	-	0	-	0	-	-	0	0	0
80	242	88	60	-	0	-	0	-	-	38	0	0
85	243	88	60	-	0	-	-	-	-	38	0	0
90	244	15	60	-	0	-	41	-	-	63	0	0
95	231	15	0	-	77	87	41	-	-	0	0	27
100	232	49	0	-	0	-	0	-	-	0	0	0
105	136	15	60	-	0	-	0	-	-	0	0	0
110	241	0	60	-	0	-	41	-	-	0	0	0
115	228	0	26	-	0	-	0	-	-	0	0	0
120	141	73	0	-	0	-	0	-	-	0	0	0
125	140	15	26	-	0	-	0	-	-	0	0	0
130	240	0	80	-	0	-	0	-	-	0	0	0
135	185	15	26	-	0	-	41	-	-	0	0	27
140	227	0	0	-	0	-	0	-	-	0	0	0
145	245	15	26	-	0	-	0	-	-	0	0	0
150	222	15	26	-	77	100	41	-	-	38	0	0
155	301	90	81	100	99	100	0	-	-	0	0	0
160	291	4	100	-	99	100	0	-	-	0	0	0

Claims

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1. A method of controlling fungus disease in plants that comprises treating the locus to be protected with an effective amount of a compound of Formula I,

10



15

I

wherein:

A is O or NR⁴;

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W is O or S;

R¹ is H; C₁ to C₆ alkyl; C₁ to C₆ haloalkyl; C₃ to C₆ cycloalkyl; C₂ to C₆ alkenyl; C₂ to C₆ alkynyl; C₂ to C₆ alkoxyalkyl; C₁ to C₃ alkyl substituted with C₃ to C₆ cycloalkyl, phenyl or benzyl, wherein said phenyl or benzyl ring is substituted on the ring with R⁶, and the benzylic carbon is substituted with R⁷;

25

R² is phenyl substituted with R⁵ and R⁶; naphthyl substituted with 1 to 2 groups selected from R⁶; thiophenyl substituted with R⁵ and R⁶; furyl substituted with R⁶; pyridyl substituted with one of the following:

R⁶, phenoxy substituted with R⁶, or phenylthio substituted with R⁶;

C₁ to C₂ alkyl substituted with phenoxy or phenylthio, said phenoxy or phenylthio being substituted on the ring with R⁶;

C₁ to C₆ alkyl; or

30

C₅ to C₇ cycloalkyl; and

R¹ and R² can be taken together, along with the carbon to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5 to 7 ring atoms in which the heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; and the carbocyclic ring can be fused with 1 or 2 R⁵-substituted benzene rings or with an R⁶-substituted thiophene ring;

R³ is phenyl substituted with R¹⁰; benzyl substituted on the benzylic carbon with a group selected from R⁷ and substituted on the phenyl ring with R¹⁰; naphthyl substituted with R¹⁰; additionally, R³ can be thiophenyl substituted with R¹⁰, furyl substituted with R¹⁰, pyridyl substituted with R¹⁰, pyrimidyl substituted with R¹⁰, or pyridazyl substituted with R¹⁰; or R³ can be C₂ to C₁₀ alkyl or C₅ to C₇ cycloalkyl;

R⁴ is hydrogen; formyl; C₂ to C₄ alkylcarbonyl; C₂ to C₄ haloalkylcarbonyl; C₂ to C₄ alkoxyalkylcarbonyl; C₂ to C₄ alkoxy carbonyl; C₂ to C₅ alkylaminocarbonyl; C₁ to C₄ alkylsulfonyl; C₁ to C₄ alkyl; C₄ to C₆ cycloalkyl; phenylaminocarbonyl where said phenyl is substituted with R¹⁰; and R⁴ can be C₃ to C₄ alkenyl or C₃ to C₄ alkynyl; or

R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a pyrrolidino, piperidino or pyrrolo ring substituted with R¹⁰, which rings can be fused to an R¹⁰-substituted benzene ring;

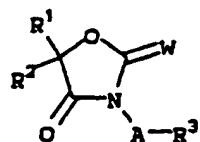
R⁵ is hydrogen; halogen; C₁ to C₁₂ alkyl; C₁ to C₁₂ haloalkyl; C₁ to C₁₂ alkoxy; C₃ to C₁₂ alkenyl; C₃ to C₁₂ haloalkenyl; C₃ to C₁₂ alkenyloxy; C₃ to C₁₂ alkynyl; C₃ to C₁₂ haloalkynyl; C₃ to C₁₂ alkylthio; C₁ to C₁₂ haloalkylthio; C₁ to C₁₂ haloalkoxy; C₁ to C₁₂ alkylsulfonyl; C₁ to C₁₂ haloalkylsulfonyl; nitro; phenyl substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; C₃ to C₁₂ alkynyoxy; C₂ to C₁₂ alkoxyalkyl; C₂ to C₁₂ alkoxyalkoxy; phenoxy methyl substituted on the phenyl ring with R⁶; benzyloxy substituted on the phenyl ring with R⁶; phenethyoxy substituted on the phenyl ring with R⁶; phenethyl substituted on the phenyl ring with R⁶; benzyl substituted on the phenyl ring with R⁶; C₂ to C₁₂ carboalkoxy; C₅ to C₆ cycloalkyl; NMe₂; or NR⁸R⁹;

R⁶ is hydrogen; 1 to 2 halogen; C₁ to C₄ alkyl; trifluoromethyl; C₁ to C₄ alkoxy; methylthio; nitro; phenoxy; C₂ to C₆ cycloalkyloxy; or C₅ to C₆ cycloalkyl;

R⁷ is hydrogen; or C₁ to C₄ alkyl;

R⁸ is H; or C₁ to C₄ alkyl;

- R⁹ is H; phenyl substituted with H; 1-2 halogen; CF₃; C₁ to C₂ alkyl; or C₁ to C₂ alkoxy; and R¹⁰ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;
- 5 provided that, when A is oxygen, R³ is phenyl substituted with R⁵ and R⁶.
2. The method of Claim 1 wherein
- A is NR⁴;
- R¹ is C₁ to C₄ alkyl; C₁ to C₃ haloalkyl; vinyl; ethynyl; or methoxymethyl;
- R² is phenyl substituted with R⁵ and R⁶; C₅ to C₇ cycloalkyl; thienyl substituted with R⁶; or pyridyl
- 10 substituted with R⁶;
- R³ is phenyl substituted with R¹⁰; and R⁴ is H; C₁ to C₃ alkyl; or C₁ to C₃ alkylcarbonyl.
3. The method of Claim 2 wherein
- R¹ is C₁ to C₄ alkyl or vinyl;
- R² is phenyl substituted with R⁵ and R⁶; R³ is phenyl substituted with 1-2 halogen, methyl or methoxy;
- 15 R⁴ is hydrogen or methyl;
- R⁵ is hydrogen; halogen; C₁ to C₄ alkyl; C₁ to C₄ haloalkyl; C₁ to C₆ alkoxy; benzyloxy; F₃CO; F₂HCO; C₁ to C₆ haloalkoxy; phenoxy substituted with R⁶; provided that if R⁵ is not H or F, then it is para to the point of attachment to the ring;
- R⁶ is hydrogen, 1 to 2 F or Cl; methyl; or methoxy; and
- 20 R⁷ is hydrogen.
4. The method of Claim 3 wherein
- R¹ is CH₃;
- R⁴ is hydrogen or methyl;
- R⁵ is H; F; Cl; CH₃; C₁ to C₆ alkoxy; or phenoxy substituted with halogen, CH₃, CH₃O or NO₂;
- 25 R⁶ is H or F; and
- R¹⁰ is F; H or CH₃.
5. The method of Claim 4, wherein the compound is selected from the class consisting of
- 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;
- 5-methyl-5-phenyl-3-(N'-phenyl-N'-methylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;
- 30 5-[4-(4-bromophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;
- 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;
- 5-(2,4-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof;
- 35 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof;
- 5-(2,5-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof;
- 5-(2-fluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof; or
- 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof; and mixtures of the foregoing.
- 40 6. A compound of the Formula IA



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wherein:

A is O or NR⁴;

W is O or S;

- R¹ is H; C₁ to C₆ alkyl; C₁ to C₆ haloalkyl; C₃ to C₆ cycloalkyl; C₂ to C₆ alkenyl; C₂ to C₆ alkynyl; C₂ to C₆ alkoxyalkyl; C₁ to C₃ alkyl substituted with C₃ to C₆ cycloalkyl, phenyl or benzyl, wherein said phenyl or benzyl ring is substituted on the ring with R⁶, and the benzylic carbon is substituted with R⁷;
- 55 R² is phenyl substituted with R⁵ and R⁶; naphthyl substituted with 1 to 2 groups selected from R⁵; thienyl substituted with R⁵ and R⁶; furyl substituted with R⁵; pyridyl substituted with one of the following:

- R⁶, phenoxy substituted with R⁶, or phenylthio substituted with R⁶;
 C₁ to C₂ alkyl substituted with phenoxy or phenylthio, said phenoxy or phenylthio being substituted on the ring with R⁶;
 C₁ to C₆ alkyl; or
 5 C₅ to C₇ cycloalkyl; and
 R¹ and R² can be taken together, along with the carbon to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5 to 7 ring atoms in which the heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; and the carbocyclic ring can be fused with 1 or 2 R⁵-substituted benzene rings or with
 10 an R⁶-substituted thiophene ring;
 R³ is phenyl substituted with R¹⁰; benzyl substituted on the benzylic carbon with a group selected from R⁷ and substituted on the phenyl ring with R¹⁰; naphthyl substituted with R¹⁰; additionally, R³ can be thienyl substituted with R¹⁰, furyl substituted with R¹⁰, pyridyl substituted with R¹⁰, pyrimidyl substituted with R¹⁰, or pyridazyl substituted with R¹⁰; or R³ can be C₂ to C₁₀ alkyl or C₅ to C₇ cycloalkyl;
 15 R⁴ is hydrogen; formyl; C₂ to C₄ alkylcarbonyl; C₂ to C₄ haloalkylcarbonyl; C₂ to C₄ alkoxyalkylcarbonyl; C₂ to C₄ alkoxy carbonyl; C₂ to C₅ alkylaminocarbonyl; C₁ to C₄ alkylsulfonyl; C₁ to C₄ alkyl; C₄ to C₆ cycloalkyl; phenylaminocarbonyl where said phenyl is substituted with R¹⁰; and R⁴ can be C₃ to C₄ alkenyl or C₃ to C₄ alkynyl; or
 R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a
 20 pyrrolidino, piperidino or pyrrolo ring substituted with R¹⁰, which rings can be fused to an R¹⁰-substituted benzene ring;
 R⁵ is hydrogen; halogen; C₁ to C₁₂ alkyl; C₁ to C₁₂ haloalkyl; C₁ to C₁₂ alkoxy; C₃ to C₁₂ alkenyl; C₃ to C₁₂ haloalkenyl; C₃ to C₁₂ alkenyloxy; C₃ to C₁₂ alkynyl; C₃ to C₁₂ haloalkynyl; C₃ to C₁₂ alkylthio; C₁ to C₁₂ haloalkylthio; C₁ to C₁₂ haloalkoxy; C₁ to C₁₂ alkylsulfonyl; C₁ to C₁₂ haloalkylsulfonyl; nitro; phenyl
 25 substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; C₃ to C₁₂ alkyloxy; C₂ to C₁₂ alkoxyalkyl; C₂ to C₁₂ alkoxyalkoxy; phenoxy methyl substituted on the phenyl ring with R⁶; benzyloxy substituted on the phenyl ring with R⁶; phenethoxy substituted on the phenyl ring with R⁶; phenethyl substituted on the phenyl ring with R⁶; benzyl substituted on the phenyl ring with R⁶; C₂ to C₁₂ carboalkoxy; C₅ to C₆ cycloalkyl; NMe₂; or NR⁸R⁹;
 30 R⁶ is hydrogen; 1 to 2 halogen; C₁ to C₄ alkyl; trifluoromethyl; C₁ to C₄ alkoxy; methylthio; nitro; phenoxy; C₂ to C₆ cycloalkyloxy; or C₅ to C₆ cycloalkyl;
 R⁷ is hydrogen; or C₁ to C₄ alkyl;
 R⁸ is H; or C₁ to C₄ alkyl;
 R⁹ is H; phenyl substituted with H; 1-2 halogen; CF₃; C₁ to C₂ alkyl; or C₁ to C₂ alkoxy; and
 35 R¹⁰ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;
 provided that
 (1) when A is O, then R³ is phenyl substituted with R⁵ or R⁶;
 40 (2) when R² is unsubstituted phenyl, then R¹ is not hydrogen, methyl or benzyl;
 (3) when R¹ is hydrogen, methyl or cyclohexyl, then R² is not methyl, isopropyl or cyclohexyl; and
 (4) R¹ and R² do not join to form -(CH₂)₅-.
7. A compound of Claim 6, wherein:
- A is NR⁴;
- 45 R¹ is C₁ to C₄ alkyl; C₁ to C₃ haloalkyl; vinyl; ethynyl; or methoxymethyl;
 R² is phenyl substituted with R⁵ and R⁶; C₅ to C₇ cycloalkyl; thiienyl substituted with R⁵; or pyridyl substituted with R⁶;
 R³ is phenyl substituted with R¹⁰; and
 R⁴ is H; C₁ to C₃ alkyl; or C₁ to C₃ alkylcarbonyl;
 50 provided that when R² is unsubstituted phenyl, R¹ is not methyl.
8. A compound of Claim 7 wherein R¹ is C₁ to C₄ alkyl or vinyl;
 R² is phenyl substituted with R⁵ and R⁶;
 R³ is phenyl substituted with 1-2 halogen, methyl or methoxy;
 R⁴ is hydrogen or methyl;
 55 R⁵ is hydrogen; halogen; C₁ to C₄ alkyl; C₁ to C₄ haloalkyl; C₁ to C₆ alkoxy; benzyloxy; F₃CO; F₂HCO; C₁ to C₆ haloalkoxy; phenoxy substituted with R⁶; provided that if R⁵ is not H or F, then it is para to the point of attachment to the ring;
 R⁶ is hydrogen, 1 to 2 F or Cl; methyl; or methoxy; and

R⁷ is hydrogen;

provided that when R² is unsubstituted phenyl, R¹ is not methyl.

9. A compound of Claim 8 wherein

R¹ is CH₃;

5 R⁴ is hydrogen or methyl;

R⁵ is H; F; Cl; CH₃; C₁ to C₆ alkoxy; or phenoxy substituted with halogen, CH₃, CH₃O or NO₂;

R⁶ is H or F; and

R¹⁰ is F; H or CH₃;

provided that R² is not unsubstituted phenyl.

10. A compound of Claim 6 selected from the class consisting of:

5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;

5-methyl-5-phenyl-3-(N-phenyl-N-methylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;

5-(4-(4-bromophenoxy)phenyl)-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;

15 5-[4-(3-fluorophenoxy)phenyl]-5-methyl-3-(phenylamino)-2-thioxo-4-oxazolidinone; and the (S)-enantiomer thereof;

5-(2,4-difluorophenyl)-5-methyl-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof;

5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione; and the (S)-enantiomer thereof;

and mixtures of the foregoing.

20 11. An agriculturally suitable composition comprising a fungicidally effective amount of a compound of Claim 6 and at least one of the following: surfactant, solid diluent or liquid diluent.

12. An agriculturally suitable composition comprising a fungicidally effective amount of a compound of Claim 7 and at least one of the following: surfactant, solid diluent or liquid diluent.

25 13. An agriculturally suitable composition comprising a fungicidally effective amount of a compound of Claim 8 and at least one of the following: surfactant, solid diluent or liquid diluent.

14. An agriculturally suitable composition comprising a fungicidally effective amount of a compound of Claim 9 and at least one of the following: surfactant, solid diluent or liquid diluent.

15. An agriculturally suitable composition comprising a fungicidally effective amount of a compound of Claim 10 and at least one of the following: surfactant, solid diluent or liquid diluent.

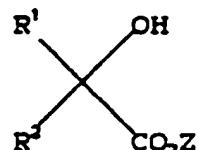
30 16. A method of controlling fungus disease in plants that comprises treating the locus to be protected with an effective amount of a combination of a compound of Formula I with cymoxanil.

17. An agriculturally suitable composition comprising a fungicidally effective amount of a combination of a compound of Claim 6 and cymoxanil and at least one of the following: surfactant, solid diluent or liquid diluent.

35 18. A process for the preparation of substituted 3-amino-2-thioxo-oxazolidin-4-ones of Formula I, comprising conducting the following reactions in an organic solvent: (1) reacting a 2-hydroxycarboxylic acid ester of Formula II with a base, (2) reacting the reaction product of (1) with carbon disulfide, (3) reacting the reaction product of (2) with an acylating agent, and (4) reacting the reaction product of (3) with a substituted hydrazine, followed by recovery of the product from the reaction mixture wherein:

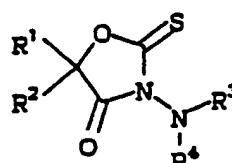
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Formula II is



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Formula (I) is



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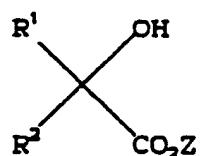
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Z is alkyl (C₁-C₁₂); alkenyl (C₃-C₄); cycloalkyl (C₃-C₁₂); cycloalkylalkyl (C₆-C₇); alkoxyalkyl (C₂-C₄); benzyl; R¹ is H; alkyl (C₁-C₆); haloalkyl (C₁-C₆); cycloalkyl (C₃-C₆); alkenyl (C₂-C₆); alkynyl (C₂-C₆); alkoxyalkyl (C₂-C₆).

- C_6); alkyl (C_1-C_3) substituted with cycloalkyl (C_3-C_6); phenyl or benzyl substituted on the ring with R^6 ; R^2 is phenyl substituted with R^5 and R^6 ; naphthyl substituted with 1-2 groups selected from R^6 ; thiienyl substituted with R^5 and R^6 ; furyl substituted with R^6 ; pyridyl substituted with R^6 , phenoxy or phenylthio; alkyl (C_1-C_6); C_5-C_7 cycloalkyl;
- 5 R¹ and R² can be taken together, along with the carbon atom to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5-7 ring atoms. The heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; the carbocyclic ring can be fused with 1-2 R⁵-substituted benzene rings or with an R⁶-substituted thiophene ring;
- 10 R³ is phenyl substituted with R⁸; benzyl substituted on the benzylic carbon with R⁷ and/or the phenyl ring with R⁸; naphthyl substituted with R⁸; thiienyl substituted with R⁸; furyl substituted with R⁸; pyridyl substituted with R⁸; pyridazyl substituted with R⁶; pyrimidyl substituted with R⁸; alkyl (C_2-C_{10}); cycloalkyl (C_5-C_7); R⁴ is H; formyl; alkylcarbonyl (C_2-C_4); haloalkylcarbonyl (C_2-C_4); alkoxyalkylcarbonyl (C_2-C_4); alkoxycarbonyl (C_2-C_4); alkylaminocarbonyl (C_2-C_5); alkylsulfonyl (C_1-C_4); alkyl (C_1-C_4); alkenyl (C_3-C_4); alkynyl (C_3-C_4); cycloalkyl (C_4-C_6); phenylaminocarbonyl wherein the phenyl is substituted with R⁸;
- 15 R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a pyrrolidino, piperidino or pyrrolo ring, which rings can be fused to an R⁸-substituted benzene ring; R⁵ is H; halogen; alkyl (C_1-C_6); haloalkyl (C_1-C_4); alkoxy (C_1-C_6); alkenyloxy (C_3-C_4); alkylthio (C_1-C_5); haloalkylthio (C_1-C_4); haloalkoxy (C_1-C_4); alkylsulfonyl (C_1-C_4); nitro; phenyl substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; alkynyloxy (C_3-C_4); alkoxyalkyl (C_2-C_6); alkoxyalkyoxy (C_2-C_6); phenoxyethyl with phenyl substituted by R⁶; benzyloxy with phenyl substituted by R⁶; phenethyloxy with phenyl substituted by R⁶; benzyl with phenyl substituted by R⁶; phenethyl with phenyl substituted by R⁶; carboalkoxy (C_2-C_6); cycloalkyl (C_5-C_6);
- 20 R⁶ is H; halogen (1-2); methyl; trifluoromethyl; alkoxy (C_1-C_4); methylthio; nitro;
- 25 R⁷ is H; or alkyl (C_1-C_4); R⁸ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;
- 30 provided that, when A is oxygen, R³ is phenyl substituted with R⁵ and R⁶.
19. A process of Claim 18 wherein the base is an alkali-metal alkoxide, hydroxide, or hydride.
20. A process of Claim 18 wherein the organic solvent is an ether, ester, amide, nitrile or a 2-hydroxycarboxylic acid ester of Formula II.
21. A process of Claim 20 wherein the organic solvent is the 2-hydroxycarboxylic acid ester of Formula II, tetrahydrofuran, N,N-dimethylformamide, N,N-dimethylacetamide, or 1-methyl-2-pyrrolidone.
- 35 22. A process of Claim 18 wherein the acylating agent is a chloroformate.
23. A process of Claim 22 wherein the acylating agent is ethyl chloroformate or methyl chloroformate.
24. A process of Claim 18 wherein the substituted hydrazine is of the formula H₂NNR³R⁴ where

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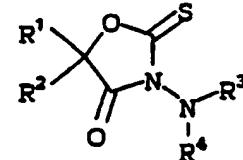
Formula II is



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Formula (I) is



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Z is alkyl (C_1-C_{12}); alkenyl (C_3-C_4); cycloalkyl (C_3-C_{12}); cycloalkylalkyl (C_6-C_7); alkoxyalkyl (C_2-C_4); benzyl; R¹ is H; alkyl (C_1-C_6); haloalkyl (C_1-C_6); cycloalkyl (C_3-C_6); alkenyl (C_2-C_6); alkynyl (C_2-C_6); alkoxyalkyl (C_2-C_6); alkyl (C_1-C_3) substituted with cycloalkyl (C_3-C_6); phenyl or benzyl substituted on the ring with R⁶;

R² is phenyl substituted with R⁵ and R⁶; naphthyl substituted with 1-2 groups selected from R⁶; thiienyl substituted with R⁵ and R⁶; furyl substituted with R⁶; pyridyl substituted with R⁶, phenoxy or phenylthio; alkyl (C₁-C₆); C₅-C₇ cycloalkyl;

5 R¹ and R² can be taken together, along with the carbon atom to which they are attached, to form a carbocyclic or heterocyclic ring (containing O, N-R⁷, or S) of 5-7 ring atoms. The heterocyclic ring can be fused with an R⁵-substituted benzene ring or an R⁶-substituted thiophene ring, the heteroatom not being attached to the spiro center; the carbocyclic ring can be fused with 1-2 R⁵-substituted benzene rings or with an R⁶-substituted thiophene ring;

10 R³ is phenyl substituted with R⁸; benzyl substituted on the benzylic carbon with R⁷ and/or the phenyl ring with R⁸; naphthyl substituted with R⁸; thiienyl substituted with R⁸; furyl substituted with R⁸; pyridyl substituted with R⁸; pyridazyl substituted with R⁶; pyrimidyl substituted with R⁸; alkyl (C₂-C₁₀); cycloalkyl (C₅-C₇);

15 R⁴ is H; formyl; alkylcarbonyl (C₂-C₄); haloalkylcarbonyl (C₂-C₄); alkoxyalkylcarbonyl (C₂-C₄); alkoxy carbonyl (C₂-C₄); alkylaminocarbonyl (C₂-C₅); alkylsulfonyl (C₁-C₄); alkyl (C₁-C₄); alkenyl (C₃-C₄); alkynyl (C₃-C₄); cycloalkyl (C₄-C₆); phenylaminocarbonyl wherein the phenyl is substituted with R⁸;

R³ and R⁴ can be taken together, along with the nitrogen atom to which they are attached, to form a pyrrolidino, piperidino or pyrrolo ring, which rings can be fused to an R⁸-substituted benzene ring;

20 R⁵ is H; halogen; alkyl (C₁-C₆); haloalkyl (C₁-C₄); alkoxy (C₁-C₆); alkenyloxy (C₃-C₄); alkylthio (C₁-C₅); haloalkylthio (C₁-C₄); haloalkoxy (C₁-C₄); alkylsulfonyl (C₁-C₄); nitro; phenyl substituted with R⁶; phenoxy substituted with R⁶; phenylthio substituted with R⁶; cyano; alkynyloxy (C₃-C₄); alkoxyalkyl (C₂-C₆); alkoxyalkyoxy (C₂-C₆); phenoxy methyl with phenyl substituted by R⁶; benzyloxy with phenyl substituted by R⁶; phenethyloxy with phenyl substituted by R⁶; benzyl with phenyl substituted by R⁶; phenethyl with phenyl substituted by R⁶; carboalkoxy (C₂-C₆); cycloalkyl (C₅-C₆);

25 R⁶ is H; halogen (1-2); methyl; trifluoromethyl; alkoxy (C₁-C₄); methylthio; nitro;

R⁷ is H; or alkyl (C₁-C₄);

30 R⁸ is 0-2 groups selected from H; CF₃; CF₃O; NO₂; CO₂Me; halogen; C₁ to C₅ alkyl; C₁ to C₅ alkoxy; or CN; provided that when the phenyl ring is disubstituted, one of the alkyl or alkoxy groups is no larger than C₁;

provided that, when A is oxygen, R³ is phenyl substituted with R⁵ and R⁶.

35 25. A process of Claim 24 wherein the substituted hydrazine is phenylhydrazine or 4-fluorophenylhydrazine.

26. A process of Claim 18 wherein:

Z is C₁-C₄ alkyl;

R¹ is methyl;

35 R² is phenyl substituted with R⁵ and R⁶;

R³ is phenyl substituted with R⁶; and

R⁴ is hydrogen.

27. A process of Claim 26 wherein Z is methyl or ethyl, R¹ is methyl, and R² is phenyl, 2,4-difluorophenyl, 4-phenoxyphenyl, 4-bromophenyl, or (3-fluorophenoxy)phenyl.

40 28. A process of Claim 18 wherein the base is potassium t-butoxide, the solvent is tetrahydrofuran, the acylating agent is ethyl chloroformate, the substituted hydrazine is phenylhydrazine, Z is methyl, R¹ is methyl, R² is phenyl, R³ is phenyl and R⁴ is hydrogen.

29. A process of Claim 18 wherein:

Reaction 1 is conducted at -80°C to 100°C;

45 Reaction 2 is conducted at -20°C to 100°C;

Reaction 3 is conducted at -20°C to 50°C; and

Reaction 4 is conducted at -20°C to 100°C.



European Patent
Office

EUROPEAN SEARCH REPORT

Application number

EP 90303859.4

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.)
			TECHNICAL FIELDS SEARCHED (Int. Cl.)
X	CHEMICAL ABSTRACTS, vol. 94, no. 21, May 25, 1981 Columbus, Ohio, USA GEFFKEN, DETLEF "Synthesis of 6,6-disubstituted 2,5-dioxodihydro-4H-1,3,4-dioxazines and their conversion to 3-amino-and 3-alkyl(aryl)-2,4-dioxotetrahydro-1,3-oxazoles." page 728, column 2, abstract -no. 175 071s & Synthesis 1981, (1), 38-40	6	C 07 D 263/44 C 07 D 413/04 C 07 D 413/12 C 07 D 495/10 A 01 N 43/76
A	<u>DE - A1 - 2 324 591</u> (BASF) * Claims 1-3 *	1-6	
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X : particularly relevant if taken alone	T : theory or principle underlying the invention		
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EP 90303859.4

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